=> D 1-37

L10 ANSWER 1 OF 37 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 1999315407 EMBASE
TI Suppression of anchorage-independent growth of human cancer cell lines by the drs gene.
AU Yamashita A.; Hakura A.; Inoue H.
CS H. Inoue, Department of Tumor Virology, Research Institute Microbial Disease, Osaka University, 3-1 Yamadaoka, Suita, Osaka 565-0871, Japan
SO Oncogene, (26 Aug 1999) 18/34 (4777-4787).
Refs: 73
ISSN: 0950-9232 CODEN: ONCNES
CY United Kingdom
DT Journal; Article
FS 016 Cancer
022 Human Genetics
029 Clinical Biochemistry
LA English
SL English

L10 ANSWER 2 OF 37 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 1
AN 1999:368611 CAPLUS
DN 131:139768
TI Thyroid hormone, T3-dependent phosphorylation and translocation of Trip230 from the Golgi complex to the nucleus
AU Chen, Yumay; Chen, Phang-Lang; Chen, Chi-Fen; Sharp, Z. Dave; Lee, Wen-Hwa
CS Department of Molecular Medicine and Institute of Biotechnology, University of Texas Health Science Center at San Antonio, San Antonio, TX, 78245-3207, USA
SO Proc. Natl. Acad. Sci. U. S. A. (1999), 96(8), 4443-4448
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English

L10 ANSWER 3 OF 37 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 2
AN 1999:222681 CAPLUS
DN 131:3357
TI Modulation of cell proliferation by cytokeratins K10 and K16
AU Paramio, Jesus M.; Casanova, M. Llanos; Segrelles, Carmen; Mittnacht, Sybille; Lane, E. Birgitte; Jorcano, Jose L.
CS Cell and Molecular Biology Program, CIEMAT, Madrid, E-28040, Spain
SO Mol. Cell. Biol. (1999), 19(4), 3086-3094
CODEN: MCEBD4; ISSN: 0270-7306
PB American Society for Microbiology
DT Journal
LA English

L10 ANSWER 4 OF 37 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 3
AN 1999:369709 CAPLUS
DN 131:143382
TI Inhibition of interleukin-6 promoter activity by the 24 kDa isoform of fibroblast growth factor-2 in HeLa cells
AU Delrieu, Isabelle; Faye, Jean-Charles; Bayard, Francis; Maret, Arlette
CS Laboratoire d'Endocrinologie et Communication Cellulaire INSERM U397, Institut Louis Bugnard, C.H.U. Rangueil, Toulouse, 31403, Fr.
SO Biochem. J. (1999), 340(1), 201-206
CODEN: BIJOAK; ISSN: 0264-6021
PB Portland Press Ltd.
DT Journal
LA English

L10 ANSWER 5 OF 37 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 4
AN 1998:608069 CAPLUS
DN 129:311634
TI Definition of a negative modulation domain in the human progesterone receptor
AU Huse, Barbara; Verca, Stefano Brenz; Matthey, Patricia; Rusconi, Sandro
CS Biochemistry Institute, Universite de Fribourg, Fribourg, CH-1700, Switz.
SO Mol. Endocrinol. (1998), 12(9), 1334-1342
CODEN: MOENEN; ISSN: 0888-8809
PB Endocrine Society
DT Journal
LA English

L10 ANSWER 6 OF 37 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 5
AN 1997:789377 CAPLUS
DN 128:99668
TI A comparative analysis of the interactions of the E6 proteins from cutaneous and genital papillomaviruses with p53 and E6AP in correlation to their transforming potential
AU Elbel, M.; Carl, S.; Spaderna, S.; Iftner, T.
CS Institut fur Kinische und Molekulare Virologie, Universitat Erlangen-Nurnberg, Erlangen, 91054, Germany
SO Virology (1997), 239(1), 132-149
CODEN: VIRLAX; ISSN: 0042-6822
PB Academic Press
DT Journal
LA English

L10 ANSWER 7 OF 37 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 6
AN 1997:478332 CAPLUS
DN 127:159300
TI Proliferation of chicken neuroretina cells induced by v-src, in vitro, depends on activation of the E2F transcription factor
AU Pasteau, Stephane; Loiseau, Laurent; Brun, Gilbert
CS Laboratoire de Biologie Moleculaire et Cellulaire de l'Ecole Normale Superieure de Lyon, UMR49 CNRS/ENS, Lyon, 69364, Fr.
SO Oncogene (1997), 15(1), 17-28
CODEN: ONCNES; ISSN: 0950-9232
PB Stockton
DT Journal
LA English

L10 ANSWER 8 OF 37 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 7
AN 1996:314940 CAPLUS
DN 125:2856
TI Inhibition of E2F activity by the cyclin-dependent protein kinase inhibitor p21 in cells expressing or lacking a functional **retinoblastoma** protein
AU Dimri, Goberdhan P.; Nakanishi, Makoto; Desprez, Pierre-Yves; Smith, James R.; Campisi, Judith
CS Dep. Cancer Biol., Univ. California, Berkeley, CA, 94720, USA
SO Mol. Cell. Biol. (1996), 16(6), 2987-2997
CODEN: MCEBD4; ISSN: 0270-7306
DT Journal
LA English

L10 ANSWER 9 OF 37 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 8
AN 1996:171410 CAPLUS
DN 124:222410
TI Adenovirus E1A activates cyclin A gene transcription in the absence of growth factors through interaction with p107
AU Zerfass, Karin; Spitkovsky, Dimitry; Schulze, Almut; Joswig, Silvia; Henglein, Berthold; Jansen-Duerr, Pidder
CS Deutsches Krebsforschungszentrum, Forschungschwerpunkt Angewandte Tumorvirologie, Heidelberg, D-69120, Germany
SO J. Virol. (1996), 70(4), 2637-42
CODEN: JOVIAM; ISSN: 0022-538X
DT Journal
LA English

L10 ANSWER 10 OF 37 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 9
AN 1996:282474 CAPLUS

DN 124:334633
TI The human papillomavirus type 16 E7 gene product interacts with and trans-activates the AP1 family of transcription factors
AU Antinore, Michael J.; Birrer, Michael J.; Patel, Daksha; Nader, Lynda; McCance, Dennis J.
CS Dep. Microbiol. Immunol., Univ. Rochester, Rochester, NY, 14642, USA
SO EMBO J. (1996), 15(8), 1950-1960
CODEN: EMJODG; ISSN: 0261-4189
DT Journal
LA English

L10 ANSWER 11 OF 37 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 10
AN 1996:624109 CAPLUS
DN 125:319634
TI A potential role for cell cycle control proteins in regulation of the cyclic adenosine 5'-monophosphate-responsive glycoprotein hormone .alpha. subunit gene
AU Pestell, Richard G.; Albanese, Chris; Lee, Richard J.; Watanabe, Genichi; Moran, Elizabeth; Johnson, Janet; Jameson, J. Larry
CS Div. Endocrinol., Metabolism, Mol. Med., Northwestern University Med. Sch., Chicago, IL, 60611, USA
SO Cell Growth Differ. (1996), 7(10), 1337-1344
CODEN: CGDIE7; ISSN: 1044-9523
DT Journal
LA English

L10 ANSWER 12 OF 37 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 11
AN 1996:733072 CAPLUS
DN 126:43469
TI Interaction of rat Cdc37-related protein with **retinoblastoma** gene product
AU Ozaki, Toshinori; Sakiyama, Shigeru
CS Division of Biochemistry, Chiba Cancer Center Research Institute, Chiba, 260, Japan
SO DNA Cell Biol. (1996), 15(11), 975-979
CODEN: DCEBE8; ISSN: 1044-5498
PB Liebert
DT Journal
LA English

L10 ANSWER 13 OF 37 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 12
AN 1996:546663 CAPLUS
DN 125:187459
TI Specific interaction of **pRB** with a rat genomic DNA fragment, REC11
AU Ozaki, Toshinori; Sakiyama, Shigeru
CS Div. Biochemistry, Chiba Cancer Center Res. Inst., Chiba, 260, Japan
SO Biochem. Biophys. Res. Commun. (1996), 226(1), 237-241
CODEN: BBRCA9; ISSN: 0006-291X
DT Journal
LA English

L10 ANSWER 14 OF 37 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 13
AN 1995:880391 CAPLUS
DN 124:2417
TI Association of human Pur.alpha. with the **retinoblastoma** protein, Rb, regulates binding to the single-stranded DNA Pur.alpha. recognition element
AU Johnson, Edward M.; Chen, Phang-Lang; Krachmarov, Chavdar P.; Barr, Sharon M.; Kanovsky, Mechael; Ma, Zhi-Wei; Lee, Wen-Hwa
CS Dep. Pathol. Brookdale Cent. Mol. Biol., Mount Sinai Sch. Med., New York, NY, 10029, USA
SO J. Biol. Chem. (1995), 270(41), 24352-60
CODEN: JBCHA3; ISSN: 0021-9258
DT Journal
LA English

L10 ANSWER 15 OF 37 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 14
AN 1995:825274 CAPLUS
DN 123:221223
TI 73-kDa heat shock cognate protein interacts directly with the N-terminal region of the **retinoblastoma** gene product **pRb**.

Identification of a novel region of **pRb**-mediating protein interaction
AU Inoue, Atsushi; Torigoe, Toshihiko; Sogahata, Katsuya; Kamiguchi, Kenjoro; Takahashi, Shuji; Sawada, Yukiharu; Saijo, Masafumi; Taya, Yoichi; Ishii, Sei-ichi; et al.
CS Dep. Pathol., Sapporo Med. Univ. Sch. Med., Sapporo, 060, Japan
SO J. Biol. Chem. (1995), 270(38), 22571-6
CODEN: JBCHA3; ISSN: 0021-9258
DT Journal
LA English

L10 ANSWER 16 OF 37 CAPLUS COPYRIGHT 2000 ACS
AN 1995:966100 CAPLUS
DN 124:47494
TI Cis-regulatory elements conferring cyclic 3',5'-adenosine monophosphate responsiveness of the progesterone receptor gene in transfected rat granulosa cells
AU Park-Sarge, Ok-Kyong; Sarge, Kevin D.
CS Dep. Physiol., Univ. Kentucky, Lexington, KY, 40536-0084, USA
SO Endocrinology (1995), 136(12), 5430-7
CODEN: ENDOAO; ISSN: 0013-7227
DT Journal
LA English

L10 ANSWER 17 OF 37 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 15
AN 1994:402362 CAPLUS
DN 121:2362
TI Identification of a novel **retinoblastoma** gene product binding site on human papillomavirus type 16 E7 protein
AU Patrick, Denis R.; Oliff, Allen; Heimbrook, David C.
CS Dep. Cancer Res., Merck Res. Lab., West Point, PA, 19486, USA
SO J. Biol. Chem. (1994), 269(9), 6842-50
CODEN: JBCHA3; ISSN: 0021-9258
DT Journal
LA English

L10 ANSWER 18 OF 37 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 16
AN 1994:551664 CAPLUS
DN 121:151664
TI Complex formation between lamin A and the **retinoblastoma** gene product: identification of the domain on lamin A required for its interaction
AU Ozaki, Toshinori; Saijo, Masafumi; Murakami, Kevin; Enomoto, Hideki; Taya, Yoichi; Sakiyama, Shigeru
CS Div. Biochemistry, Chiba Cancer Center Res. Inst., Chiba, 260, Japan
SO Oncogene (1994), 9(9), 2649-53
CODEN: ONCNES; ISSN: 0950-9232
DT Journal
LA English

L10 ANSWER 19 OF 37 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 17
AN 1994:267126 CAPLUS
DN 120:267126
TI Induction of apoptosis by adenovirus type 5 E1A in rat cells requires a proliferation block
AU Mymryk, Joe S.; Shire, Kathryn; Bayley, Stanley T.
CS Dep. Biochem., McMaster Univ., Hamilton, ON, L8S 4K1, Can.
SO Oncogene (1994), 9(4), 1187-93
CODEN: ONCNES; ISSN: 0950-9232
DT Journal
LA English

L10 ANSWER 20 OF 37 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 18
AN 1994:674816 CAPLUS
DN 121:274816
TI Nuclear localization and transforming activity of human papillomavirus type 16 E7-.beta.-galactosidase fusion protein: characterization of the nuclear localization sequence
AU Fujikawa, Kiyomi; Furuse, Mikio; Uwabe, Kenichiro; Maki, Hideo; Yoshie, Osamu
CS Shionogi Inst. Med. Sci., Osaka, 566, Japan
SO Virology (1994), 204(2), 789-93

CODEN: VIRLAX; ISSN: 0042-6822
DT Journal
LA English

L10 ANSWER 21 OF 37 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 19
AN 1993:492576 CAPLUS
DN 119:92576
TI EBNA-5, an Epstein-Barr virus-encoded nuclear antigen, binds to the **retinoblastoma** and p53 proteins
AU Szekely, Laszlo; Selivanova, Galina; Magnusson, Kristinn P.; Klein, George; Wiman, Klas G.
CS Dep. Tumor Biol., Karolinska Inst., Stockholmd, S-104 01, Swed.
SO Proc. Natl. Acad. Sci. U. S. A. (1993), 90(12), 5455-9
CODEN: PNASA6; ISSN: 0027-8424
DT Journal
LA English

L10 ANSWER 22 OF 37 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 20
AN 1993:406147 CAPLUS
DN 119:6147
TI Induction of the cell cycle in baby rat kidney cells by adenovirus type 5 E1A in the absence of E1B and a possible influence of p53
AU Shepherd, Susan E.; Howe, John A.; Mymryk, Joe S.; Bayley, Stanley T.
CS Dep. Biol., McMaster Univ., Hamilton, ON, L8S 4K1, Can.
SO J. Virol. (1993), 67(5), 2944-9
CODEN: JOVIAM; ISSN: 0022-538X
DT Journal
LA English

L10 ANSWER 23 OF 37 CAPLUS COPYRIGHT 2000 ACS
AN 1993:618974 CAPLUS
DN 119:218974
TI Transcriptional inhibition by the **retinoblastoma** protein
AU Fattaey, Ali; Helin, Kristian; Harlow, Ed
CS Cancer Cent., Massachusetts Gen. Hosp., Charlestown, MA, 02129, USA
SO Philos. Trans. R. Soc. London, Ser. B (1993), 340(1293), 333-6
CODEN: PTRBAE; ISSN: 0080-4622
DT Journal
LA English

L10 ANSWER 24 OF 37 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 21
AN 1993:78234 CAPLUS
DN 118:78234
TI Biological function of the **retinoblastoma** protein requires distinct domains for hyperphosphorylation and transcription factor binding
AU Qian, Yongyi; Luckey, Carol; Horton, Lynn; Esser, Mark; Templeton, Dennis J.
CS Inst. Pathol., Case West. Reserve Univ., Cleveland, OH, 44106, USA
SO Mol. Cell. Biol. (1992), 12(12), 5363-72
CODEN: MCEBD4; ISSN: 0270-7306
DT Journal
LA English

L10 ANSWER 25 OF 37 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 22
AN 1993:227284 CAPLUS
DN 118:227284
TI E1A-responsive elements for repression of rat fibronectin gene transcription
AU Nakajima, Takuma; Nakamura, Takeshi; Tsunoda, Shiho; Nakada, Susumu; Oda, Kinichiro
CS Nichirei Res. Inst., Tokyo, 189, Japan
SO Mol. Cell. Biol. (1992), 12(6), 2837-46
CODEN: MCEBD4; ISSN: 0270-7306
DT Journal
LA English

L10 ANSWER 26 OF 37 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 23
AN 1993:3767 CAPLUS
DN 118:3767
TI Ability of adenovirus 5 E1A proteins to suppress differentiation of BC3H1 myoblasts correlates with their binding to a 300 kDa cellular protein
AU Mymryk, Joe S.; Lee, Raymond W. H.; Bayley, Stanley T.

CS Dep. Biochem., McMaster Univ., Hamilton, ON, L8S 4K1, Can.
SO Mol. Biol. Cell (1992), 3(10), 1107-15
CODEN: MBCEEV; ISSN: 1059-1524
DT Journal
LA English

L10 ANSWER 27 OF 37 CAPLUS COPYRIGHT 2000 ACS
AN 1991:507519 CAPLUS
DN 115:107519
TI Negative regulation of human c-fos expression by the **retinoblastoma** gene product [Erratum to document cited in CA113(15):127563t]
AU Robbins, Paul D.; Horowitz, Jonathan M.; Mulligan, Richard C.
CS Whitehead Inst. Biomed. Res., Cambridge, MA, 02142, USA
SO Nature (London) (1991), 351(6325), 419
CODEN: NATUAS; ISSN: 0028-0836
DT Journal
LA English

L10 ANSWER 28 OF 37 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 24
AN 1991:179512 CAPLUS
DN 114:179512
TI A very large spontaneous deletion at aprt locus in CHO cells: sequence similarities with small aprt deletions
AU Dewyse, Pascale; Bradley, W. E. C.
CS Inst. Cancer Montreal, Sherbrooke, PQ, H2L 4M1, Can.
SO Somatic Cell Mol. Genet. (1991), 17(1), 57-68
CODEN: SCMGDN; ISSN: 0740-7750
DT Journal
LA English

L10 ANSWER 29 OF 37 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 91306145 EMBASE
DN 1991306145
TI A role for both RB and p53 in the regulation of human cellular senescence.
AU Shay J.W.; Pereira-Smith O.M.; Wright W.E.
CS Dept. of Cell Biol./Neurosci., The University of Texas, Southwestern Medical Center, 5323 Harry Hines Boulevard,Dallas, TX 75235, United States
SO Experimental Cell Research, (1991) 196/1 (33-39).
ISSN: 0014-4827 CODEN: ECREAL
CY United States
DT Journal; Article
FS 016 Cancer
029 Clinical Biochemistry
LA English
SL English

L10 ANSWER 30 OF 37 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 25
AN 1991:38032 CAPLUS
DN 114:38032
TI Hyperphosphorylation of the **retinoblastoma** gene product is determined by domains outside the simian virus 40 large-T-antigen-binding regions
AU Hamel, Paul A.; Cohen, Brenda L.; Sorce, Lilly M.; Gallie, Brenda L.; Phillips, Robert A.
CS Res. Inst., Hosp. Sick Child., Toronto, ON, M5G 1X8, Can.
SO Mol. Cell. Biol. (1990), 10(12), 6586-95
CODEN: MCEBD4; ISSN: 0270-7306
DT Journal
LA English

L10 ANSWER 31 OF 37 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 26
AN 1989:148853 CAPLUS
DN 110:148853
TI Cellular targets for transformation by the adenovirus E1A proteins
AU Whyte, Peter; Williamson, Nicola M.; Harlow, Ed
CS Cold Spring Harbor Lab., Cold Spring Harbor, NY, 11724, USA
SO Cell (Cambridge, Mass.) (1989), 56(1), 67-75
CODEN: CELLB5; ISSN: 0092-8674
DT Journal
LA English

L10 ANSWER 32 OF 37 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 27
AN 1988:199309 CAPLUS
DN 108:199309
TI Human **retinoblastoma** susceptibility gene: genomic organization and analysis of heterozygous intragenic **deletion mutants**
AU Bookstein, Robert; Lee, Eva Y. H. P.; To, Hoang; Young, Lih Jiuan; Sery, Theodore W.; Hayes, Robert C.; Friedmann, Theodore; Lee, Wen Hwa
CS Sch. Med., Univ. California San Diego, La Jolla, CA, 92093, USA
SO Proc. Natl. Acad. Sci. U. S. A. (1988), 85(7), 2210-14
CODEN: PNASA6; ISSN: 0027-8424
DT Journal
LA English

L10 ANSWER 33 OF 37 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 28
AN 1988:566918 CAPLUS
DN 109:166918
TI SV40 large tumor antigen forms a specific complex with the product of the **retinoblastoma** susceptibility gene
AU DeCaprio, James A.; Ludlow, John W.; Figge, James; Shew, Jin Yuh; Huang, Chun Ming; Lee, Wen Hwa; Marsilio, Erika; Paucha, Eva; Livingston, David M.
CS Dana-Farber Cancer Inst., Harvard Med. Sch., Boston, MA, 02115, USA
SO Cell (Cambridge, Mass.) (1988), 54(2), 275-83
CODEN: CELLB5; ISSN: 0092-8674
DT Journal
LA English

L10 ANSWER 34 OF 37 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1988:326801 BIOSIS
DN BR35:32135
TI HUMAN **RETINOBLASTOMA** SUSCEPTIBILITY GENE GENOMIC ORGANIZATION AND ANALYSIS OF HETEROZYGOUS INTRAGENIC **DELETION MUTANTS**
.
AU BOOKSTEIN R; LEE E Y-H P; TO H; YOUNG L-J; LEE W-H
CS DEP. PATHOL. M-012, UNIV. CALIF., SAN DIEGO, LA JOLLA, CALIF. 92093.
SO SYMPOSIUM ON THE MOLECULAR BIOLOGY OF THE EYE: GENES, VISION AND OCULAR DISEASE HELD AT THE 17TH ANNUAL UCLA (UNIVERSITY OF CALIFORNIA-LOS ANGELES) MEETING ON MOLECULAR AND CELLULAR BIOLOGY, SANTA FE, NEW MEXICO, USA, FEBRUARY 6-12, 1988. J CELL BIOCHEM SUPPL. (1988) 0 (12 PART B), 233.
CODEN: JCBSD7.
DT Conference
FS BR; OLD
LA English

L10 ANSWER 35 OF 37 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 29
AN 1986:547520 CAPLUS
DN 105:147520
TI Molecular cloning of the human esterase D gene, a genetic marker of **retinoblastoma**
AU Lee, Eva Y. H. P.; Lee, Wen Hwa
CS Sch. Med., Univ. California, San Diego, La Jolla, CA, 92093, USA
SO Proc. Natl. Acad. Sci. U. S. A. (1986), 83(17), 6337-41
CODEN: PNASA6; ISSN: 0027-8424
DT Journal
LA English

L10 ANSWER 36 OF 37 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 30
AN 1985:450954 CAPLUS
DN 103:50954
TI Truncated gag-related proteins are produced by large **deletion mutants** of Rous sarcoma virus and form virus particles
AU Voynow, Susan L.; Coffin, John M.
CS Sch. Med., Tufts Univ., Boston, MA, 02111, USA
SO J. Virol. (1985), 55(1), 79-85
CODEN: JOVIAM; ISSN: 0022-538X
DT Journal
LA English

L10 ANSWER 37 OF 37 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 31
AN 1985:448942 CAPLUS
DN 103:48942
TI Evolutionary variants of Rous sarcoma virus: large **deletion**

mutants do not result from homologous recombination
AU Voynow, Susan L.; Coffin, John M.
CS Sch. Med., Tufts Univ., Boston, MA, 02111, USA
SO J. Virol. (1985), 55(1), 67-78
CODEN: JOVIAM; ISSN: 0022-538X
DT Journal
LA English

=> D HIS

(FILE 'HOME' ENTERED AT 09:42:34 ON 24 FEB 2000)

FILE 'REGISTRY' ENTERED AT 09:44:51 ON 24 FEB 2000
L1 1 S 212254-43-8

FILE 'MEDLINE' ENTERED AT 09:45:56 ON 24 FEB 2000
L2 0 S 212254-43-8
L3 0 S L1
L4 8321 S RETINOBLASTOMA OR PRB\
L5 8321 S RETINOBLASTOMA OR PRB
L6 3696 S DELETION MUTANTS
L7 3696 S (DELETION MUTANTS)
L8 37 S L5 AND L7

FILE 'CAPLUS, BIOSIS, EMBASE' ENTERED AT 10:02:01 ON 24 FEB 2000
L9 97 S L8
L10 37 DUP REM L9 (60 DUPLICATES REMOVED)

=> D L10 24, 30 BIB ABS

L10 ANSWER 24 OF 37 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 21
AN 1993:78234 CAPLUS
DN 118:78234
TI Biological function of the **retinoblastoma** protein requires distinct domains for hyperphosphorylation and transcription factor binding
AU Qian, Yongyi; Luckey, Carol; Horton, Lynn; Esser, Mark; Templeton, Dennis J.
CS Inst. Pathol., Case West. Reserve Univ., Cleveland, OH, 44106, USA
SO Mol. Cell. Biol. (1992), 12(12), 5363-72
CODEN: MCEBD4; ISSN: 0270-7306
DT Journal
LA English
AB Despite the importance of the **retinoblastoma** susceptibility gene to tumor growth control, the structural features of its encoded protein (**pRb**) and their relationship to protein function have not been well explored. We constructed a panel of **deletion mutants** of **pRb** expression vectors and used a biol. assay for **pRb** that measures growth inhibition and morphol. changes in **pRb** -transfected Saos-2 cells to correlate structural alterations of the **pRb** coding region with function. We tested the deleted proteins for the ability to bind to viral oncoprotein E1A and to the transcription factor E2F. We also measured the ability of the mutant proteins to become hyperphosphorylated in vivo and to be recognized as substrates in vitro by a cell cycle-regulatory kinase assocd. with cyclin A. We identified two regions of **pRb** that are required for E2F binding and for hyperphosphorylation. E1A binding domains partially overlap but are distinct from both of these other two regions. Biol. function of **pRb** is dependent on retention of the integrity of both of these biochem. defined domains. These data support the model that **pRb** is a transducer of afferent signals (via the kinase that phosphorylates it) and efferent signals (through transcription factor binding), using distinct structural elements. Preservation of both of these features is essential for the ability of **pRb** to induce growth inhibition and morphol. changes upon reintroduction into transfected cells.

L10 ANSWER 30 OF 37 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 25
AN 1991:38032 CAPLUS
DN 114:38032
TI Hyperphosphorylation of the **retinoblastoma** gene product is

determined by domains outside the simian virus 40 large-T-antigen-binding regions

AU Hamel, Paul A.; Cohen, Brenda L.; Sorce, Lilly M.; Gallie, Brenda L.; Phillips, Robert A.

CS Res. Inst., Hosp. Sick Child., Toronto, ON, M5G 1X8, Can.

SO Mol. Cell. Biol. (1990), 10(12), 6586-95
CODEN: MCEBD4; ISSN: 0270-7306

DT Journal

LA English

AB With the murine **retinoblastoma** (RB) cDNA, a series of RB mutants were expressed in COS-1 cells and the **pRB** products were assessed for their ability (i) to bind to large T antigen (large T), (ii) to become modified by phosphorylation, and (iii) to localize in the nucleus. All point mutations and deletions introduced into regions previously defined as contributing to binding to large T abolished **pRB**-large T complex formation and prevented hyperphosphorylation of the RB protein. In contrast, a series of deletions 5' to these sites did not interfere with binding to large T. While some of the 5' **deletion mutants** were clearly phosphorylated in a cell cycle-dependent manner, one, .DELTA.Pvu, failed to be phosphorylated despite binding to large T. A **pRB** with mutations created at three putative p34cdc2 phosphorylation sites in the N-terminal region behaved similarly to wild-type **pRB**, whereas the construct .DELTA.P5-6-7-8, mutated at four serine residues C terminal to the large T-binding site, failed to become hyperphosphorylated despite retaining the ability to bind large T. All of the mutants described were also found to localize in the nucleus. These results demonstrate that the domains in **pRB** responsible for binding to large T are distinct from those recognized by the relevant pRB-specific kinase(s) and/or those which contain cell cycle-dependent phosphorylation sites. Furthermore, these data are consistent with a model in which cell cycle-dependent phosphorylation of **pRB** requires complex formation with other cellular proteins.

L17 ANSWER 2 OF 56 CAPLUS COPYRIGHT 2000 ACS
AN 1998:649243 CAPLUS
DN 130:12022
TI **pRB** plays an essential role in cell cycle arrest induced by DNA damage
AU Harrington, Elizabeth A.; Bruce, Jacqueline L.; Harlow, Ed; Dyson, Nicholas
CS Laboratory of Molecular Oncology, MGH Cancer Center, Charlestown, MA, 02129, USA
SO Proc. Natl. Acad. Sci. U. S. A. (1998), 95(20), 11945-11950
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA

L17 ANSWER 4 OF 56 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1999:306750 BIOSIS
DN PREV199900306750
TI **Cancer therapy** based on p53.
AU McCormick, Frank (1)
CS (1) Cancer Research Institute, 2340 Sutter Street, San Francisco, CA, 94115 USA
SO Cancer Journal from Scientific American, (**May-June, 1999**) Vol. 5, No. 3, pp. 139-151.
ISSN: 1081-4442.
DT Article
LA English

L17 ANSWER 29 OF 56 USPATFULL
AN 1999:18714 USPATFULL
TI Gene therapy methods and compositions
IN Oin, Xiao-Oiang, Brighton, MA, United States
PA Biogen, Inc, Cambridge, MA, United States (U.S. corporation)
PI US 5869040 19990209 <--
AI US 1995-481814 19950607 (8)
DT Utility
LN.CNT 2515
INCL INCLM: 424/093.210
INCLS: 435/069.100; 435/320.100; 435/366.000; 536/023.500
NCL NCLM: 424/093.210
NCLS: 435/069.100; 435/320.100; 435/366.000; 536/023.500
IC [6]
ICM: A01N063-00
EXF 435/172.3; 435/240.1; 435/240.2; 435/252.2; 435/252.3; 435/320.1; 435/6; 435/69.7; 435/69.1; 435/366; 536/24.1; 536/24.31; 536/27; 536/23.5; 514/44; 424/93.21
C

L17 ANSWER 32 OF 56 USPATFULL
AN 1998:159923 USPATFULL
TI Therapeutic use of the **retinoblastoma susceptibility** gene product
IN Lee, Wen-Hwa, San Antonio, TX, United States
Lee, Eva Y-H.P., San Antonio, TX, United States
Goodrich, David W., Houston, TX, United States
Shepard, H. Michael, Rancho Santa Fe, CA, United States
Wang, Nan Ping, Seattle, WA, United States
Johnson, Duane, Encinitas, CA, United States
PA The Regents of the University of California, Oakland, CA, United States (U.S. corporation)
Canji, Inc., San Diego, CA, United States (U.S. corporation)
PI US 5851991 19981222 <--
AI US 1994-306513 19940913 (8)
RLI Continuation-in-part of Ser. No. US 1993-121108, filed on 13 Sep 1993, now abandoned Ser. No. Ser. No. US 1992-956472, filed on 2 Oct 1992, now abandoned And Ser. No. US 1993-126810, filed on 24 Sep 1993, now abandoned which is a continuation of Ser. No. US 1991-778510, filed on 17 Oct 1991, now abandoned which is a continuation-in-part of Ser. No. US 1987-91547, filed on 31 Aug 1987, now patented, Pat. No. US 5011773, issued on 30 Apr 1991 Ser. No. Ser. No. US 1987-98612, filed on 17 Sep 1987, now patented, Pat. No. US 4942123, issued on 17 Jul 1990 Ser. No. Ser. No. US 1990-550877, filed on 11 Jul 1990, now abandoned Ser. No. Ser. No. US 1990-553892, filed on 16 Jul 1990, now abandoned Ser. No. Ser. No. US 1987-108748, filed on 15 Oct 1987, now abandoned Ser. No. Ser. No. US 1988-265829, filed on 31 Oct 1988, now abandoned And Ser. No. US 1990-553905, filed on 16 Jul 1990, now abandoned , said Ser. No. US -121108 which is a continuation-in-part of Ser. No. US 1993-79207, filed on 17 Jun 1993, now abandoned which is a continuation of Ser. No. US 1992-914039, filed on 14 Jul 1992, now abandoned which is a continuation of Ser. No. US -550877 which is a division of Ser. No. US -98612 , said Ser. No. US -956472 which is a continuation of Ser. No. US -553892 which is a continuation-in-part of Ser. No. US -91547 Ser. No. Ser. No. US -98612 Ser. No. Ser. No. US -108748 Ser. No. Ser. No. US -265829 And Ser. No. US -553905
DT Utility
LN.CNT 3788

L17 ANSWER 43 OF 56 USPATFULL
AN 97:109711 USPATFULL
TI CDK4 binding assay
IN Draetta, Giulio, Winchester, MA, United States
Gyuris, Jeno, Winchester, MA, United States
PA Mitotix, Inc., Cambridge, MA, United States (U.S. corporation)
PI US 5691147 19971125 <--
AI US 1994-253155 19940602 (8)
DT Utility
LN.CNT 2332
INCL INCLM: 435/007.100
INCLS: 436/501.000; 530/300.000; 530/350.000; 536/023.100; 536/023.500; 435/004.000
NCL NCLM: 435/007.100
NCLS: 435/004.000; 436/501.000; 530/300.000; 530/350.000; 536/023.100; 536/023.500
IC [6]
ICM: G01N033-53
EXF 435/4; 435/7.1; 536/23.1; 536/23.5; 530/300; 530/350; 436/501
C

L17 ANSWER 48 OF 56 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 2000113663 EMBASE
TI Gene therapy: Designer promoters for tumour targeting.
AU Nettelbeck D.M.; Jerome V.; Muller R.
CS D.M. Nettelbeck, Inst. Molecular Biology/Tumor Res., Philipps-University Marburg, Emil-Mannkopff-Strasse 2, D-35033 Marburg, Germany. nettelbeck@imt.uni-marburg.de
SO Trends in Genetics, (1 Apr 2000) 16/4 (174-181).
Refs: 73
ISSN: 0168-9525 CODEN: TRGEE2
PUI S 0168-9525(99)01950-2
CY United Kingdom
DT Journal; General Review
FS 016 Cancer
022 Human Genetics
029 Clinical Biochemistry
LA English
S

L17 ANSWER 51 OF 56 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 2000028926 EMBASE
TI A paradigm for cancer treatment using the retinoblastoma gene in a mouse model.
AU Yu Nikitin A.; Riley D.J.; Lee W.-H.
CS W.-H. Lee, Institute of Biotechnology, The University of Texas, Health Science Center, 15355 Lambda Drive, San Antonio, TX 78245-3207, United States. leew@uthscsa.edu
SO Annals of the New York Academy of Sciences, (1999) 886/- (12-22).
Refs: 74
ISSN: 0077-8923 CODEN: ANYAA
CY United States
DT Journal; Conference Article
FS 016 Cancer
LA English
SL English

=> d bib abs l22

L22 ANSWER 1 OF 1 MEDLINE DUPLICATE 1
AN 93296157 MEDLINE
DN 93296157
TI EBNA-5, an Epstein-Barr virus-encoded nuclear antigen, binds to the retinoblastoma and p53 proteins.
AU Szekely L; Selivanova G; Magnusson K P; Klein G; Wiman K G
CS Department of Tumor Biology, Karolinska Institute, Stockholm, Sweden.
NC 2 R01 CA14054-19 (NCI)
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1993 Jun 15) 90 (12) 5455-9.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199309
AB Epstein-Barr virus (EBV) immortalized human lymphoblastoid cell lines express six virally encoded nuclear proteins, designated EBV nuclear antigens 1-6 (EBNA-1-6). We show that the EBNA-5 protein (alternatively designated EBNA-LP) that is required for B-cell transformation can form a molecular complex with the **retinoblastoma** (RB) and p53 **tumor suppressor proteins**. Using EBNA-5 **deletion** mutants, we have found that a 66-amino acid-long peptide, encoded by the W repeat of the EBV genome, is sufficient for binding. Point mutations of RB and p53 that inhibit their complexing with other DNA viral oncoproteins do not affect their binding to EBNA-5. p53 competes with RB for EBNA-5 binding. Our data suggest that the mechanisms involved in EBV transformation may include impairment of RB and p53 function.

=> d bib abs hitstr l12 1-4

L12 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2000 ACS
AN 1997:7594 HCAPLUS
DN 126:116335
TI Expression of the retinoblastoma (RB) tumor suppressor gene inhibits tumor cell invasion in vitro
AU Li, Jian; **Hu, Shi-Xue**; Perng, Guang-Shing; **Zhou, Yunli**; Xu, Kai; Zhang, Chunyan; Seigne, John; **Benedict, William F.**; **Xu, Hong-Ji**
CS Dep. Molecular Oncology, Univ. Texas M. D. Anderson Cancer Center, Houston, TX, 77030, USA
SO Oncogene (1996), 13(11), 2379-2386
CODEN: ONCNES; ISSN: 0950-9232
PB Stockton
DT Journal
LA English
AB To det. if replacement of the retinoblastoma (RB) tumor suppressor gene could inhibit invasion of RB-defective tumor cells, the capacity of tumor cells to migrate or invade was quantitated by the Boyden chamber assay. The studies were done in a diverse group of stable RB-reconstituted human tumor cell lines, including those derived from the osteosarcoma and carcinomas of the lung, breast and bladder. The expression of the exogenous wild-type RB protein in these tumor cell lines was driven by either a constitutively active promoter or an inducible promoter. It was found that significantly more tumor cells from the parental RB-defective cell lines and the RB- revertants than from the RB-reconstituted RB+ cell lines penetrated through the Matrigel (two-tailed t-test), although both RB+ and RB- migrated at approx. the same rate on uncoated polycarbonate filters in the Boyden chambers. Of note, the inhibition of invasiveness of various RB-defective tumor cells by RB replacement was apparently well correlated with suppression of their tumorigenicity in vivo. In contrast, although either functional RB or p53 re-expression effectively suppressed tumor formation in nude mice of the RB-/p53null osteosarcoma cell line, Saos-2, replacement of the wild-type p53 gene had much less impact on their invasiveness as compared to the RB gene. These studies provided an insight into the broader biol. basis of the RB-mediated tumor suppression in RB-defective tumor cells.

L12 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2000 ACS
AN 1996:299875 HCAPLUS
DN 125:1299
TI Enhanced tumor suppressor gene therapy via replication-deficient adenovirus vectors expressing an N-terminal truncated retinoblastoma protein
AU **Xu, Hong-Ji**; **Zhou, Yunli**; Seigne, John; Perng, Guang-Shing; Mixon, Michael; Zhang, Chunyan; Li, Jian; **Benedict, William F.**; **Hu, Shi-Xue**
CS Dep. Molecular Oncology, Hematology, Urology, Univ. Texas M.D. Anderson Cancer Center, Hoston, TX, 77030, USA
SO Cancer Res. (1996), 56(10), 2245-2249
CODEN: CNREA8; ISSN: 0008-5472
DT Journal
LA English
AB The preclin. studies presented here demonstrate that treatment of human non-small cell lung carcinoma and bladder carcinoma cells by a recombinant adenovirus vector, AdCMVpRB94, expressing the N-terminal truncated retinoblastoma (RB) protein (pRB94) completely suppressed the tumorigenicity of the treated tumor cells in nude mice. Furthermore, gene therapy of established human RB- and RB+ bladder xenograft cancers in nude mice by AdCMVpRB94 resulted in regression of the treated tumors. Of note, although both the full-length and the truncated forms of the RB protein, when overexpressed in tumor cells via replication-deficient adenovirus vectors, were capable of suppression of tumor growth, the pRB94 was evidently more potent than the full-length RB protein.

L12 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2000 ACS
AN 1994:698069 HCAPLUS
DN 121:298069

TI Enhanced tumor cell growth suppression by an N-terminal truncated retinoblastoma protein
AU **Xu, Hong-Ji**; Xu, Kai; **Zhou, Yunli**; Li, Jian; **Benedict, William F.**; **Hu, Shi-Xue**
CS Center for Biotechnology, Baylor College of Medicine, The Woodlands, TX, 77381, USA
SO Proc. Natl. Acad. Sci. U. S. A. (1994), 91(21), 9837-41
CODEN: PNASA6; ISSN: 0027-8424
DT Journal
LA English
AB The retinoblastoma (RB) gene encodes a nuclear phosphoprotein of 928 amino acids (pRB). Thus far, much effort in RB research has been focused on both the viral oncoprotein-binding domains and the C-terminal domain, whereas little is known about the N-terminal moiety of the protein. The authors report here that an N-terminal truncated RB protein of .apprxeq.94 kDa (pRB94) exerts more potent cell growth suppression as compared to the full-length pRB protein in a diversity of tumor cell lines examd., including those having a normal endogenous RB gene. Tumor cells transfected with the pRB94-expressing plasmids displayed multiple morphol. changes frequently assocd. with cellular senescence and/or apoptosis. They failed to enter S phase and rapidly died. The pRB94 expressed in recipient tumor cells had a longer half-life than the full-length pRB protein and tended to remain in an active un- or hypophosphorylated form. Since it has also been found that N-terminal truncated RB proteins often accumulated in growth-arrested and/or differentiated tumor cells, the authors suggest that N-terminal truncation of pRB may be one of the cellular mechanisms modulating the RB protein function in cell-cycle control.

L12 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2000 ACS
AN 1994:400412 HCAPLUS
DN 121:412
TI Further characterization of retinoblastoma gene-mediated cell growth and tumor suppression in human cancer cells
AU **Zhou, Yunli**; Li, Jian; Xu, Kai; **Hu, Shi Xue**; **Benedict, William F.**; **Xu, Hong Ji**
CS Center Biotechnology, Baylor Coll. Med., Woodlands, TX, 77381, USA
SO Proc. Natl. Acad. Sci. U. S. A. (1994), 91(10), 4165-9
CODEN: PNASA6; ISSN: 0027-8424
DT Journal
LA English
AB The authors have transfected the osteosarcoma cell line Saos2 and the bladder carcinoma cell line 5637 with addnl. retinoblastoma (RB) expression plasmids. The RB-reconstituted Saos2 and 5637 cells showed only slightly lower ratios of cells undergoing DNA synthesis compared to their parental RB- tumor cells, and there were no noticeable changes in cell morphol. Furthermore, the authors have isolated long-term RB+ clones from Saos2, 5637, and the retinoblastoma cell line WERI-Rb27 after transfection/transduction with a RB expression plasmid or retrovirus. These clones were similar to their parental cell lines in terms of morphol. and growth rates, and they all expressed functional RB protein (p110RB) as evidenced by its potential of phosphorylation, simian virus 40 large tumor antigen binding, and nuclear tethering. No mutation or deletion of the exogenous RB gene was detectable by PCR and single-strand conformation polymorphism anal. In addn., either the individual or pooled RB+ clones did form malignant tumors in nude mice but usually with a longer latency period and lower frequency. Such tumors also retained normal RB expression, suggesting that at least a portion of the RB-reconstituted tumor cells were still tumorigenic. This phenomenon is referred to by the authors as tumor suppressor resistance (TSR).

=> d bib abs l18 1-26

L18 ANSWER 1 OF 26 HCAPLUS COPYRIGHT 2000 ACS
AN 2000:11274 HCAPLUS
TI Human cells compromised for p53 function exhibit defective global and transcription-coupled nucleotide excision repair, whereas cells compromised for pRb function are defective only in global repair
AU Therrien, Jean-Philippe; Drouin, Regen; Baril, Caroline; Drobetsky, Elliot A.
CS Division of Pathology, Department of Medical Biology, Faculty of Medicine, Laval University and Unite de Recherche en Genetique Humaine et Moleculaire, Research Centre, Centre Hospitalier Universitaire de Quebec, PQ, G1L 3L5, Can.
SO Proc. Natl. Acad. Sci. U. S. A. (1999), 96(26), 15038-15043
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
AB After exposure to DNA-damaging agents, the p53 tumor suppressor protects against neoplastic transformation by inducing growth arrest and apoptosis. A series of investigations has also demonstrated that, in UV-exposed cells, p53 regulates the **removal** of DNA photoproducts from the genome overall (global nucleotide excision repair), but does not participate in an overlapping pathway that **removes** damage specifically from the transcribed strand of active genes (transcription-coupled nucleotide excision repair). Here, the highly sensitive ligation-mediated PCR was employed to quantify, at nucleotide resoln., the repair of UVB-induced cyclobutane pyrimidine dimers (CPDs) in genetically p53-deficient Li-Fraumeni skin fibroblasts, as well as in human lung fibroblasts expressing the human papillomavirus (HPV) E6 oncoprotein that functionally inactivates p53. Lung fibroblasts expressing the HPV E7 gene product, which similarly inactivates the **retinoblastoma tumor-suppressor protein** (pRb), were also investigated. PRb acts downstream of p53 to mediate G1 arrest, but has no demonstrated role in DNA repair. Relative to normal cells, HPV E6-expressing lung fibroblasts and Li-Fraumeni skin fibroblasts each manifested defective CPD repair along both the transcribed and nontranscribed strands of the p53 and/or c-jun loci. HPV E7-expressing lung fibroblasts also exhibited reduced CPD **removal**, but only along the nontranscribed strand. Our results provide striking evidence that transcription-coupled repair, in addn. to global repair, are p53-dependent in UV-exposed human fibroblasts. Moreover, the obsd. DNA-repair defect in HPV E7-expressing cells reveals a function for this oncoprotein in HPV-mediated carcinogenesis, and may suggest a role for pRb in global nucleotide excision repair.

L18 ANSWER 2 OF 26 HCAPLUS COPYRIGHT 2000 ACS
AN 1999:777719 HCAPLUS
DN 132:89178
TI Activation of the cyclin D1 gene by the E1A-associated protein p300 through AP-1 inhibits cellular apoptosis
AU Albanese, Chris; D'Amico, Mark; Reutens, Anne T.; Fu, Maofu; Watanabe, Genichi; Lee, Richard J.; Kitsis, Richard N.; Henglein, Berthold; Avantaggiati, Maria; Somasundaram, Kumaravel; Thimmapaya, Bayar; Pestell, Richard G.
CS Albert Einstein Cancer Center, Department of Developmental and Molecular Biology, Albert Einstein College of Medicine, Bronx, NY, 10461, USA
SO J. Biol. Chem. (1999), 274(48), 34186-34195
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB The adenovirus E1A protein interferes with regulators of apoptosis and growth by phys. interacting with cell cycle regulatory **proteins** including the **retinoblastoma tumor suppressor protein** and the coactivator proteins p300/CBP (where CBP is the CREB-binding protein). The p300/CBP proteins occupy a pivotal role in regulating mitogenic signaling and apoptosis. The mechanisms by which cell cycle control genes are directly regulated by p300 remain to be detd.

The cyclin D1 gene, which is overexpressed in many different tumor types, encodes a regulatory subunit of a holoenzyme that phosphorylates and inactivates pRB. In the present study E1A12S inhibited the cyclin D1 promoter via the amino-terminal p300/CBP binding domain in human choriocarcinoma JEG-3 cells. P300 induced cyclin D1 protein abundance, and p300, but not CBP, induced the cyclin D1 promoter. Cyclin D1 or p300 overexpression inhibited apoptosis in JEG-3 cells. The CH3 region of p300, which was required for induction of cyclin D1, was also required for the inhibition of apoptosis. P300 activated the cyclin D1 promoter through an activator protein-1 (AP-1) site at -954 and was identified within a DNA-bound complex with c-Jun at the AP-1 site. Apoptosis rates of embryonic fibroblasts derived from mice homozygously **deleted** of the cyclin D1 gene (cyclin D1-/-) were increased compared with wild type control on several distinct matrixes. P300 inhibited apoptosis in cyclin D1+/+ fibroblasts but increased apoptosis in cyclin D1-/- cells. The anti-apoptotic function of cyclin D1, demonstrated by sub-G1 anal. and annexin V staining, may contribute to its cellular transforming and cooperative oncogenic properties.

L18 ANSWER 3 OF 26 HCAPLUS COPYRIGHT 2000 ACS
AN 1999:641971 HCAPLUS
TI A genetic screen for modifiers of E2F in Drosophila melanogaster
AU Staehling-Hampton, Karen; Ciampa, Phillip J.; Brook, Adam; Dyson, Nicholas
CS Massachusetts General Hospital Cancer Center, Charlestown, MA, 02129, USA
SO Genetics (1999), 153(1), 275-287
CODEN: GENTAE; ISSN: 0016-6731
PB Genetics Society of America
DT Journal
LA English
AB The activity of the E2F transcription factor is regulated in part by pRB, the **protein** product of the **retinoblastoma tumor suppressor** gene. Studies of tumor cells show that the p16ink4a/cdk4/cyclin D/pRB pathway is mutated in most forms of cancer, suggesting that the deregulation of E2F, and hence the cell cycle, is a common event in tumorigenesis. Extragenic mutations that enhance or suppress E2F activity are likely to alter cell-cycle control and may play a role in tumorigenesis. We used an E2F overexpression phenotype in the Drosophila eye to screen for **modifiers** of E2F activity. Coexpression of dE2F and its heterodimeric partner dDP in the fly eye induces S phases and cell death. We isolated 33 enhancer mutations of this phenotype by EMS and X-ray mutagenesis and by screening a deficiency library collection. The majority of these mutations sorted into six complementation groups, five of which have been identified as alleles of brahma (brm), moira (mor) osa, pointed (pnt), and polycephalon (poc). Osa, brm, and mor encode proteins with homol. to SWI1, SWI2, and SWI3, resp., suggesting that the activity of a SWI/SNF chromatin-remodeling complex has an important impact on E2F-dependent phenotypes. Mutations in poc also suppress phenotypes caused by p21CIP1 expression, indicating an important role for polycephalon in cell-cycle control.

L18 ANSWER 4 OF 26 HCAPLUS COPYRIGHT 2000 ACS
AN 1999:515993 HCAPLUS
DN 131:270009
TI The 100-kDa Proteolytic Fragment of RB Is Retained Predominantly within the Nuclear Compartment of Apoptotic Cells
AU Chen, Wei-dong; Geradts, Joseph; Keane, Maccon M.; Lipkowitz, Stanley; Zajac-Kaye, Maria; Kaye, Frederic J.
CS Medicine Branch, Division of Clinical Sciences, National Cancer Institute, Bethesda, MD, 20889, USA
SO Mol. Cell Biol. Res. Commun. (1999), 1(3), 216-220
CODEN: MCBCFS; ISSN: 1522-4724
PB Academic Press
DT Journal
LA English
AB The **retinoblastoma tumor suppressor protein** (RB) has been shown to play a role in regulating the eukaryotic cell cycle, promoting cellular differentiation, and modulating programmed cell death. Although regulation of RB tumor suppressor activity is mediated by reversible phosphorylation, an addnl. posttranslational **modification** involves the cleavage of 42

residues from the carboxy-terminus of RB during the onset of drug-induced or receptor-mediated apoptosis. We now demonstrate that a recombinant p100c1 RB species localizes to the nucleus, where it may retain wildtype "pocket" protein binding activity. In addn., using immunocytochem., we show that cleavage of the endogenous RB protein occurs in vivo in human cells and that p100c1 is predominantly retained within the nuclear compartment of cells during early apoptosis. We also show that the carboxy-terminal cleavage of RB is detected immediately following caspase-3 and PARP cleavage during FAS-mediated apoptosis of MCF10 cells. These findings suggest that this cleavage event may be a component of a downstream cascade during programmed cell death. (c) 1999 Academic Press.

L18 ANSWER 5 OF 26 HCAPLUS COPYRIGHT 2000 ACS
AN 1999:368611 HCAPLUS
DN 131:139768
TI Thyroid hormone, T3-dependent phosphorylation and translocation of Trip230 from the Golgi complex to the nucleus
AU Chen, Yumay; Chen, Phang-Lang; Chen, Chi-Fen; Sharp, Z. Dave; Lee, Wen-Hwa
CS Department of Molecular Medicine and Institute of Biotechnology, University of Texas Health Science Center at San Antonio, San Antonio, TX, 78245-3207, USA
SO Proc. Natl. Acad. Sci. U. S. A. (1999), 96(8), 4443-4448
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
AB Trip230 is a novel coactivator of the thyroid hormone receptor that is neg. regulated by the **retinoblastoma tumor-suppressor protein**. In an examn. of its subcellular distribution, Trip230 localized predominantly to the vicinity of the Golgi instead of the nucleus, as other nuclear hormone receptor coactivators. Using a series of **deletion** mutants, a crit. region identified for Golgi area targeting coincided with a previously defined thyroid hormone receptor-binding domain of Trip230. During cell cycle progression, the expression level of Trip230 is const. and a significant portion is imported into the nucleus at S phase. Within an hour of treating cells with T3, Trip230 immunofluorescence transiently colocalized with TR in prominent subnuclear structures. T3-dependent nuclear import of Trip230 does not require new protein synthesis. Coincident with T3 treatment and nuclear import, newly phosphorylated residue(s) appeared in Trip230, suggesting that phosphorylation may be involved in its nuclear import. These findings provided a novel mechanism for the regulation of nuclear hormone transcription factors by hormone-responsive phosphorylation and nuclear import of cytoplasmically located coactivators.

L18 ANSWER 6 OF 26 HCAPLUS COPYRIGHT 2000 ACS
AN 1999:198446 HCAPLUS
DN 130:350569
TI The retinoblastoma protein alters the phosphorylation state of polyomavirus large T antigen in murine cell extracts and inhibits polyomavirus origin DNA replication
AU Reynisdottir, Inga; Bhattacharyya, Subarna; Zhang, Dong; Prives, Carol
CS Department of Biological Sciences, Columbia University, New York, NY, 10027, USA
SO J. Virol. (1999), 73(4), 3004-3013
CODEN: JOVIAM; ISSN: 0022-538X
PB American Society for Microbiology
DT Journal
LA English
AB The **retinoblastoma tumor suppressor protein** (pRb) can assoc. with the transforming proteins of several DNA tumor viruses, including the large T antigen encoded by polyomavirus (Py T Ag). Although pRb function is crit. for regulating progression from G1 to S phase, a role for pRb in S phase has not been demonstrated or excluded. To identify a potential effect of pRb on DNA replication, pRb protein was added to reaction mixts. contg. Py T Ag, Py origin-contg. DNA (Py ori-DNA), and murine FM3A cell exts. We found that pRb strongly represses Py ori-DNA replication in vitro. Unexpectedly, however, this inhibition only partially depends on the interaction of pRb with Py T Ag,

since a mutant Py T Ag (dl141) lacking the pRb interaction region was also significantly inhibited by pRb. This result suggests that pRb interferes with or alters one or more components of the murine cell replication ext. Furthermore, the ability of Py T Ag to be phosphorylated in such exts. is markedly reduced in the presence of pRb. Since cyclin-dependent kinase (CDK) phosphorylation of Py T Ag is required for its replication function, we hypothesize that pRb interferes with this phosphorylation event. Indeed, the S-phase CDK complex (cyclin A-CDK2), which phosphorylates both pRb and Py T Ag, alleviates inhibition caused by pRb. Moreover, hyperphosphorylated pRb is incapable of inhibiting replication of Py ori-DNA in vitro. We propose a new requirement for maintaining pRb phosphorylation in S phase, namely, to prevent **deleterious** effects on the cellular replication machinery.

L18 ANSWER 7 OF 26 HCAPLUS COPYRIGHT 2000 ACS
AN 1999:169835 HCAPLUS
DN 131:28553
TI Mechanism of transcriptional repression of E2F by the retinoblastoma tumor suppressor protein
AU Ross, John F.; Liu, Xuan; Dynlacht, Brian David
CS Department of Molecular and Cellular Biology, Harvard University, Cambridge, MA, 02138, USA
SO Mol. Cell (1999), 3(2), 195-205
CODEN: MOCEFL; ISSN: 1097-2765
PB Cell Press
DT Journal
LA English
AB The **retinoblastoma tumor suppressor protein** (pRB) is a transcriptional repressor, crit. for normal cell cycle progression. We have undertaken studies using a highly purified reconstituted in vitro transcription system to demonstrate how pRB can repress transcriptional activation mediated by the E2F transcription factor. Remarkably, E2F activation became resistant to pRB-mediated repression after the establishment of a partial (TFIIA/TFIID) preinitiation complex (PIC). DNase I footprinting studies suggest that E2F recruits TFIID to the promoter in a step that also requires TFIIA and confirm that recruitment of the PIC by E2F is blocked by pRB. These studies suggest a detailed mechanism by which E2F activates and pRB represses transcription without the requirement of histone-**modifying** enzymes.

L18 ANSWER 8 OF 26 HCAPLUS COPYRIGHT 2000 ACS
AN 1999:95922 HCAPLUS
DN 130:265679
TI Re-expression of endogenous p16ink4a in oral squamous cell carcinoma lines by 5-aza-2'-deoxycytidine treatment induces a senescence-like state
AU Timmermann, Stefanie; Hinds, Philip W.; Munger, Karl
CS Pathology Department and Harvard Center for Cancer Biology, Harvard Medical School, Boston, MA, 02115, USA
SO Oncogene (1998), 17(26), 3445-3453
CODEN: ONCNES; ISSN: 0950-9232
PB Stockton Press
DT Journal
LA English
AB The authors have previously reported that a set of oral squamous cell carcinoma lines express specifically elevated cdk6 activity. One of the cell lines, SCC4, contains a cdk6 amplification and expresses functional p16ink4a, the other cell lines express undetectable levels of p16ink4a, despite a lack of coding-region mutations. Two of the cell lines, SCC15 and SCC40 have a hypermethylated p16ink4A promoter and a third cell line, SCC9, has a mutation in the p16ink4a promoter. Using the demethylation agent 5-aza-2'-deoxycytidine, the authors showed that the p16ink4a protein was re-expressed after a 5-day treatment with this chem. One cell line, SCC15 expressed high levels of p16ink4a. In this line, cdk6 activity was decreased after 5-aza-2'deoxycytidine treatment, and the hypophosphorylated, growth **suppressive** form of the **retinoblastoma tumor suppressor protein** pRB was detected. Expression of p16ink4a persisted; even after the drug was **removed** and the cells expressed senescence-assocd. .beta.-galactosidase activity. Ectopic expression of

p16ink4a with a recombinant retrovirus in this cell line also induced a similar senescence-like phenotype. Hence, it was possible to restore a functional pRB pathway in an oral squamous cell carcinoma line by inducing re-expression of endogenous p16ink4a in response to treatment with a demethylating agent.

L18 ANSWER 9 OF 26 HCAPLUS COPYRIGHT 2000 ACS
AN 1998:90731 HCAPLUS
DN 128:179325
TI TCR antigen-induced cell death occurs from a late G1 phase cell cycle check point
AU Lissy, Natalie A.; Van Dyk, Linda F.; Becker-Hapak, Michelle; Vocero-Akbani, Adita; Mendler, Jason H.; Dowdy, Steven F.
CS Howard Hughes Medical Institute and Division of Molecular Oncology, Departments of Pathology and Medicine Washington University School of Medicine, St. Louis, MO, 63110, USA
SO Immunity (1998), 8(1), 57-65
CODEN: IUNIEH; ISSN: 1074-7613
PB Cell Press
DT Journal
LA English
AB **Deletion** of antigen-activated T cells after an immune response and during peripheral neg. selection after strong T cell receptor (TCR) engagement of cycling T cells occurs by an apoptotic process termed TCR antigen-induced cell death (AID). By analyzing the timing of death, cell cycle markers, BrdU-labeled S phase cells, and phase-specific centrifugally elutriated cultures from stimulated Jurkat T cells and peripheral blood lymphocytes, the authors found that AID occurs from a late G1 check point prior to activation of cyclin E:Cdk2 complexes. T cells stimulated to undergo AID can be rescued by effecting an early G1 block by direct transduction of p16INK4a tumor suppressor protein or by inactivation of the **retinoblastoma tumor suppressor protein** (pRb) by transduced HPV E7 protein. These results suggest that AID occurs from a late G1 death check point in a pRb-dependent fashion.

L18 ANSWER 10 OF 26 HCAPLUS COPYRIGHT 2000 ACS
AN 1997:694814 HCAPLUS
DN 128:19298
TI G1 control gene status is frequently altered in resectable non-small cell lung cancer
AU Betticher, Daniel C.; White, Gavin R. M.; Vonlanthen, Silvia; Liu, Xuan; Kappeler, Andreas; Altermatt, Hans J.; Thatcher, Nick; Heighway, Jim
CS Institute of Medical Oncology, Inselspital, University of Bern, Bern, Switz.
SO Int. J. Cancer (1997), 74(5), 556-562
CODEN: IJCNAW; ISSN: 0020-7136
PB Wiley-Liss
DT Journal
LA English
AB Progression through the mammalian cell cycle is controlled by a series of cyclins, cyclin-dependent kinases (cdks) and cdk inhibitors. Cyclin D1, cdk4 and the **tumor suppressors** p16 and **retinoblastoma protein** (pRb) are thought to comprise a linked system governing cell passage through the G1 phase of the cell cycle. Extending an earlier study on cyclin D1 expression, a series of resectable non-small cell lung carcinomas (NSCLCs) was examd. for defects in other elements of this control system. Forty-six of fifty-one NSCLC specimens exhibited at least one alteration of these cell-cycle regulators. Immunohistochem. anal. revealed that 33% and 47% of the tumors failed to express pRb and p16, resp. Failure to detect pRb did not correlate with loss of heterozygosity at the RB1 locus. Eleven of 12 tumors showing pos. (normal) pRb staining over-expressed nuclear localized cyclin D1, including 8 with amplification of the cyclin D1 gene (CCND1). However, in a no. of lesions (n = 5) where cyclin D1 was over-expressed but localized to the cytoplasm, pRb expression was undetectable. Sequencing of exons 1 and 2 of the p16 gene (CDKN2) revealed 3/51 tumors with somatic mutations (in addn. to 1 case with a germ-line alteration). All of these lesions were pos. for p 16 protein. No clear homozygous **deletions** of CDKN2 were obsd. by multiplex PCR. As assessed by

immunostaining using a p16 monoclonal antibody, there was an inverse correlation of pRb and p16 down-regulation. While patients with tumors over-expressing cyclin D1 had a significantly lower incidence of local relapse, the group whose tumors failed to express pRb had a significantly greater risk of local relapse and tended to have shortened event-free survival. Our data show that alteration of at least one cell cycle-regulator gene occurs in the majority of resectable NSCLCs.

L18 ANSWER 11 OF 26 HCAPLUS COPYRIGHT 2000 ACS
AN 1997:572837 HCAPLUS
DN 127:245483
TI RRB1 and RRB2 encode maize retinoblastoma-related proteins that interact with a plant D-type cyclin and geminivirus replication protein
AU Ach, Robert A.; Durfee, Tim; Miller, Ann B.; Taranto, Patti; Hanley-Bowdoin, Linda; Zambryski, Patricia C.; Gruissem, Wilhelm
CS Department of Plant and Microbial Biology, University of California, Berkeley, CA, 94720-3102, USA
SO Mol. Cell. Biol. (1997), 17(9), 5077-5086
CODEN: MCEBD4; ISSN: 0270-7306
PB American Society for Microbiology
DT Journal
LA English
AB Unlike mammalian and yeast cells, little is known about how plants regulate G1 progression and entry into the S phase of the cell cycle. In mammalian cells, a key regulator of this process is the **retinoblastoma tumor suppressor protein** (RB). In contrast, G1 control in Saccharomyces cerevisiae does not utilize an RB-like protein. We report here the cloning of cDNAs from two Zea mays genes, RRB1 and RRB2, that encode RB-related proteins. Further, RRB2 transcripts are alternatively splices to yield two proteins with different C termini. At least one RRB gene is expressed in all the tissues examd., with the highest levels seen in the shoot apex. RRB1 is a 96-kDa nuclear protein that can phys. interact with two mammalian DNA tumor virus oncoproteins, simian virus 40 large-T antigen and adenovirus E1A, and with a plant D-type cyclin. These assocns. are abolished by mutation of a conserved cysteine residue in RRB1 that is also essential for RB function. RRB1 binding potential is also sensitive to **deletions** in the conserved A and B domains, although difference exist in these effects compared to those of human RB. RRB1 can also bind to the AL1 protein from tomato golden mosaic virus (TGMV), a protein which is essential for TGMV DNA replication. These results suggest that G1 regulation in plant cells is controlled by a mechanism which is much more similar to that found in mammalian cells than that in yeast.

L18 ANSWER 12 OF 26 HCAPLUS COPYRIGHT 2000 ACS
AN 1997:514694 HCAPLUS
DN 127:215354
TI The phosphatase inhibitor okadaic acid stimulates the TSH-induced G1-S phase transition in thyroid cells
AU Lazzereschi, Davide; Coppa, Anna; Mincione, Gabriella; Lavitrano, Marialuisa; Fragomele, Francesco; Colletta, Giulia
CS Dipartimento di Medicina Sperimentale e Patologia, Facolta di Medicina e Chirurgia, Universita "La Sapienza", Rome, Italy
SO Exp. Cell Res. (1997), 234(2), 425-433
CODEN: ECREAL; ISSN: 0014-4827
PB Academic
DT Journal
LA English
AB Protein phosphorylation plays an essential role in regulating many cellular processes in eukaryotes. Signal transduction mechanisms that are reversibly controlled by protein phosphorylation also require protein phosphatases (PPs). Okadaic acid (OA), which is a potent inhibitor of protein phosphatase 2A (PP2A) and protein phosphatase 1, elicits phosphorylation of many proteins in unstimulated cells and induces different cellular responses, including transcriptional activation, shape changes, and pseudomitotic state. In this study, the effects of OA on rat thyroid cells (FRTL-5 strain) were analyzed to evaluate the role of serine/threonine phosphatases in hormone-induced thyroid cell proliferation. OA at a concn. range between 0.1 and 1 nM stimulated thyroid cell growth. Furthermore, 0.25 nM OA increased about 3.5-fold the

TSH-induced DNA synthesis in quiescent cells. OA treatment also stimulated cell proliferation induced by drugs that mimic TSH effect, such as 8-Br-cAMP and cholera toxin, suggesting that PP2A activity was relevant in the cAMP pathway activated by the hormone. Flow cytometry expts. showed that OA significantly increased the fraction of TSH-stimulated quiescent cells entering the S phase. In order to define the mechanisms underlying the obsd. stimulatory effect of OA on thyroid cell growth, expression of genes relevant in the G1-S phase transition was evaluated. A 2-fold increase in the level of cyclin D1 mRNA expression was found by Northern blot anal. in OA-treated cells. Although cdk2 gene expression was not modulated by the same OA treatment, an increase in Cdk2 protein was revealed by immunopptn. expts. Moreover, OA **modifies** the phosphorylation pattern of the **tumor suppressor retinoblastoma protein**, a key event in the G1-S phase transition. Therefore, these expts. reveal that PP2A phosphatases play an important role in thyroid cell growth and can act at multiple sites in the TSH pathways driving cells to S phase.

L18 ANSWER 13 OF 26 HCAPLUS COPYRIGHT 2000 ACS
AN 1997:514675 HCAPLUS
DN 127:215892
TI Inhibition of mouse thymidylate synthase promoter activity by the wild-type p53 tumor suppressor protein
AU Lee, Yuandan; Chen, Yan; Chang, Long-Sheng; Johnson, Lee F.
CS Department of Molecular Genetics, Children's Hospital, The Ohio State University, Columbus, OH, 43210, USA
SO Exp. Cell Res. (1997), 234(2), 270-276
CODEN: ECREAL; ISSN: 0014-4827
PB Academic
DT Journal
LA English
AB The p53 tumor suppressor protein is an important neg. regulator of the G1 to S transition in mammalian cells. We have investigated the effect of p53 on the expression of the mouse thymidylate synthase (TS) gene, which normally increases as cells enter S phase. A luciferase indicator gene that was driven by the wild-type or various **modified** forms of the TATA-less mouse TS promoter was transiently cotransfected with a p53 expression plasmid into TS-deficient hamster V79 cells and the level of luciferase activity was detd. We found that wild-type p53 inhibited TS promoter activity by greater than 95% but had a strong stimulatory effect on an artificial promoter that contained multiple p53-binding sites. In contrast, an expression plasmid that encodes a mutant form of p53 or a wild-type **retinoblastoma tumor suppressor protein** had little effect on TS promoter activity. **Deletion** of sequences upstream or downstream of the TS essential promoter region, or inactivation of each of the known elements within the essential promoter region, had no effect on the ability of wild-type p53 to inhibit TS promoter activity. Our observations indicate that the inhibition of TS promoter activity by p53 is not due to the presence of a specific p53 neg. response element in the TS promoter. Rather, it appears that p53 inhibits the TS promoter by sequestering ("squelching") one or more general transcription factors.

L18 ANSWER 14 OF 26 HCAPLUS COPYRIGHT 2000 ACS
AN 1997:465286 HCAPLUS
DN 127:188048
TI Both conserved region 1 (CR1) and CR2 of the human papillomavirus type 16 E7 oncogene are required for induction of epidermal hyperplasia and tumor formation in transgenic mice
AU Gulliver, Gene A.; Herber, Renee L.; Liem, Amy; Lambert, Paul F.
CS McArdle Lab. Cancer Res., Univ. Wisconsin Med. Sch., Madison, WI, 53706, USA
SO J. Virol. (1997), 71(8), 5905-5914
CODEN: JOVIAM; ISSN: 0022-538X
PB American Society for Microbiology
DT Journal
LA English
AB High-risk human papillomavirus type 16 (HPV-16) and HPV-18 are assocd. with the majority of human cervical carcinomas, and 2 viral genes, HPV E6 and E7, are commonly found to be expressed in these cancers. The presence

of HPV-16 E7 is sufficient to induce epidermal hyperplasia and epithelial tumors in transgenic mice. In this study, expts. were performed in transgenic mice to det. which domains of E7 contribute to these in vivo properties. The human keratin 14 promoter was used to direct expression of mutant E7 genes to stratified squamous epithelia in mice. The E7 mutants chosen had either an in-frame **deletion** in the conserved region 2 (CR2) domain, which is required for binding of the **retinoblastoma tumor suppressor protein** (pRb) and pRb-like proteins, or an in-frame **deletion** in the E7 CR1 domain. The CR1 domain contributes to cellular transformation at a level other than pRb binding. Four lines of animals transgenic for an HPV-16 E7 harboring a CR1 **deletion** and 5 lines harboring a CR2 **deletion** were generated and were obsd. for overt and histol. phenotypes. A detailed time course anal. was performed to monitor acute effects of wild-type vs. mutant E7 on the epidermis, a site of high-level expression. In the transgenic mice with the wild-type E7 gene, age-dependent expression of HPV-16 E7 correlated with the severity of epidermal hyperplasia. Similar age-dependent patterns of expression of the mutant E7 genes failed to result in any phenotypes. In addn., the transgenic mice with a mutant E7 gene did not develop tumors. These expts. indicate that binding and inactivation of pRb and pRb-like proteins through the CR2 domain of E7 are necessary for induction of epidermal hyperplasia and carcinogenesis in mouse skin and also suggest a role for the CR1 domain in the induction of these phenotypes through as-yet-uncharacterized mechanisms.

L18 ANSWER 15 OF 26 HCAPLUS COPYRIGHT 2000 ACS
AN 1997:392955 HCAPLUS
DN 127:79505
TI Induction of p16 during immortalization by HPV 16 and 18 and not during malignant transformation
AU Nakao, Y.; Yang, X.; Yokoyama, M.; Ferenczy, A.; Tang, S. C.; Pater, M. M.; Pater, A.
CS Division of Basic Medical Sciences, Faculty of Medicine, Memorial University of Newfoundland, St John's, NF, A1B 3V6, Can.
SO Br. J. Cancer (1997), 75(10), 1410-1416
CODEN: BJCAAI; ISSN: 0007-0920
PB Churchill Livingstone
DT Journal
LA English
AB The p16 (MTS1) tumor-suppressor gene is a cyclin-dependent kinase (cdk) inhibitor that decelerates the cell cycle by inactivating the cdks that phosphorylate the **retinoblastoma tumor-suppressor** gene (Rb) **protein** (pRb). In cervical cancers, pRb is inactivated by the HPV E7 oncoprotein or by mutations. The hypothesis of earlier reports was that the disruption of the p16/cdk-cyclin/Rb cascade is essential for malignant cervical transformation/carcinogenesis. The authors previously established in vitro model systems of cervical cancer representing four steps of oncogenic progression initiated by the two most common oncogenic HPVs in ectocervical and endocervical epithelial cells. This report used these systems to investigate the role of p16 in cervical cancers. A dramatic enhancement of the p16 RNA level was obsd. after immortalization by HPV 16 or 18. Furthermore, the p16 protein was newly obsd. following immortalization. However, no further changes were found for RNA or protein levels after serum selection or malignant transformation. For three cervical carcinoma cell lines, similar high levels of p16 expression were seen. Point mutations or homozygous **deletions** of p16 were not obsd. in the in vitro systems or in clin. specimens. These results suggest that the inactivation of the p16/cdk-cyclin/Rb cascade does not occur during malignant transformation but occurs during the immortalization by HPV in HPV-harboring premalignant lesions, the in situ equiv. of immortalized cells. Also suggested is that p16 has no role in the specific malignant transformation step from immortal premalignant lesions during the carcinogenesis of HPV-initiated cervical cancers.

L18 ANSWER 16 OF 26 HCAPLUS COPYRIGHT 2000 ACS
AN 1997:252145 HCAPLUS
DN 126:327832
TI Accumulation of p53 induced by the adenovirus E1A protein requires regions

involved in the stimulation of DNA synthesis
AU Querido, Emmanuelle; Teodoro, Jose G.; Branton, Philip E.
CS Dep. Biochemistry, McGill Univ., Montreal, PQ, H3G 1Y6, Can.
SO J. Virol. (1997), 71(5), 3526-3533
CODEN: JOVIAM; ISSN: 0022-538X
PB American Society for Microbiology
DT Journal
LA English
AB It has been known for some time that expression of the 243-residue (243R) human adenovirus type 5 (Ad5) early region 1A (E1A) protein causes an increase in the level of the cellular tumor suppressor p53 and induction of p53-dependent apoptosis. **Deletion** of a portion of conserved region 1 (CR1) had been shown to prevent apoptosis, suggesting that binding of p300 and/or the pRB **retinoblastoma tumor suppressor** and related **proteins** might be implicated. To examine the mechanism of the E1A-induced accumulation of p53, cells were infected with viruses expressing E1A-243R contg. various **deletions** which have well-characterized effects on p300 and pRB binding. It was found that in human HeLa cells and rodent cells, complex formation with p300 but not pRB was required for the rise in p53 levels. However, in other human cell lines, including MRC-5 cells, E1A proteins which were able to form complexes with either p300 or pRB induced a significant increase in p53 levels. Only E1A mutants defective in binding both classes of proteins were unable to stimulate p53 accumulation. This same pattern was also apparent in p53-null mouse cells coinfected by Ad5 mutants and an adenovirus vector expressing either wild-type or mutant human p53 under a cytomegalovirus promoter, indicating that the difference in importance of pRB binding may relate to differences between rodent and human p53 expression. The increase in p53 levels correlated well with the induction of apoptosis and, as shown previously, with the stimulation of cellular DNA synthesis. Thus, it is possible that the accumulation of p53 is induced by the induction of unscheduled DNA synthesis by E1A proteins and that increased levels of p53 then activate cell death pathways.

L18 ANSWER 17 OF 26 HCAPLUS COPYRIGHT 2000 ACS
AN 1996:725736 HCAPLUS
DN 126:45658
TI The tumorigenic potential and cell growth characteristics of p53-deficient cells are equivalent in the presence or absence of Mdm2
AU Jones, Stephen N.; Sands, Arthur T.; Hancock, Amy R.; Vogel, Hannes; Donehower, Lawrence A.; Linke, Steven P.; Wahl, Geoffrey M.; Bradley, Allan
CS Dep. Mol. Human Genet., Baylor Coll. Med., Houston, TX, 77030, USA
SO Proc. Natl. Acad. Sci. U. S. A. (1996), 93(24), 14106-14111
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
AB The Mdm2 oncoprotein forms a complex with the p53 tumor suppressor protein and inhibits p53-mediated regulation of heterologous gene expression. Recently, Mdm2 has been found to bind several other proteins that function to regulate cell cycle progression, including the E2F-1/DP1 transcription factor complex and the **retinoblastoma tumor-suppressor protein**. To det. whether Mdm2 plays a role in cell cycle control or tumorigenesis that is distinct from its ability to modulate p53 function, the authors have examd. and compared both the in vitro growth characteristics of p53-deficient and Mdm2/p53-deficient fibroblasts, and the rate and spectrum of tumor formation in p53-deficient and Mdm2/p53-deficient mice. The authors find no difference between p53-deficient fibroblasts and Mdm2/p53-deficient fibroblasts either in their rate of proliferation in culture or in their survival frequency when treated with various genotoxic agents. Cell cycle studies indicate no difference in the ability of the two cell populations to enter S phase when treated with DNA-damaging agents or nucleotide antimetabolites, and p53-deficient fibroblasts and Mdm2/p53-deficient fibroblasts exhibit the same rate of spontaneous immortalization following long-term passage in culture. Finally, p53-deficient mice and Mdm2/p53-deficient mice display the same incidence and spectrum of spontaneous tumor formation in vivo. These results demonstrate that **deletion** of Mdm2 has no addnl. effect on cell proliferation, cell cycle control, or tumorigenesis when

p53 is absent.

L18 ANSWER 18 OF 26 HCAPLUS COPYRIGHT 2000 ACS
AN 1996:640465 HCAPLUS
DN 125:271925
TI Skeletal muscle cells lacking the retinoblastoma protein display defects in muscle gene expression and accumulate in S and G2 phases of the cell cycle
AU Novitch, Bennett G.; Mulligan, George J.; Jacks, Tyler; Lassar, Andrew B.
CS Dep. Biol. Chem. Molecular Pharmacol., Harvard Med. Sch., Boston, MA, 02115, USA
SO J. Cell Biol. (1996), 135(2), 441-456
CODEN: JCLBA3; ISSN: 0021-9525
DT Journal
LA English
AB Viral oncoproteins that inactivate the **retinoblastoma tumor suppressor protein** (pRb) family both block skeletal muscel differentiation and promote cell cycle progression. To clarify the dependence of terminal differentiation on the presence of the different pRb-related proteins, myogenesis was studied using isogenic primary fibroblasts derived from mouse embryos individually deficient for pRb, p107, or p130. When ectopically expressed in skeletal muscle differentiation program characterized by normal expression of early differentiation markers such as myogenin and p21, but attenuated expression of late differentiation markers such as myosin heavy chain (MHC). Similar defects in MHC expression were not obsd. in cells lacking either p107 or p130, indicating that the defect is specific to the loss of pRb. In contrast to wild-type, p107-deficient, or p130-deficient differentiated myocytes that are permanently withdrawn from the cell cycle, differentiated myocytes lacking pRb accumulate in S and G2 phases and express extremely high levels of cyclins A and B, cyclin-dependent kinase (Cdk2), and Cdc2, but fail to readily proceed to mitosis. Administration of caffeine, an agent that **removes** inhibitory phosphorylations on inactive Cdc2/cyclin B complexes, specifically induced mitotic catastrophe in pRb-deficient myocytes, consistent with the observation that the majority of pRb-deficient myocytes arrest in S and G2. Together, these findings indicate that pRb is required for the expression of late skeletal muscle differentiation markers and for the inhibition of DNA synthesis, but that a pRb-independent mechanism restricts entry of differentiated myocytes into mitosis.

L18 ANSWER 19 OF 26 HCAPLUS COPYRIGHT 2000 ACS
AN 1996:367125 HCAPLUS
DN 125:78217
TI SV40 large T antigen transactivates the human cdc2 promoter by inducing a CCAAT box binding factor
AU Chen, Haifeng; Campisi, Judith; Padmanabhan, R.
CS Med. Cent., Univ. Kansas, Kansas City, KS, 66160-7421, USA
SO J. Biol. Chem. (1996), 271(24), 13959-13967
CODEN: JBCHA3; ISSN: 0021-9258
DT Journal
LA English
AB Cyclin-dependent protein kinases (Cdks) play a key role in the cell division cycle of eukaryotic cells. Cdc2, the first mammalian Cdk that was discovered, is expressed in S phase and functions in the G2 to M phase transition. By transfecting segments of the human cdc2 promoter linked to a reporter gene into monkey kidney (CV-1) cells, we identified the region contg. the SP1, E2F, and two CCAAT box binding sites as essential and sufficient for basal transcription. SV40 large T antigen (SV40-LT) is a viral oncoprotein that transactivates viral and cellular promoters and induces DNA synthesis in quiescent cells. SV40-LT transactivated wild-type cdc2 promoter/reporter constructs in a dose-dependent manner, coinciding with an increase in endogenous cdc2 mRNA. A mutant promoter from which the two CCAAT box motifs were **deleted** was 8-fold less sensitive to SV40-LT. Activation by SV40-LT did not require its ability to bind the **retinoblastoma** or p53 **tumor suppressor proteins**. SV40-LT induced a specific CCAAT box-binding factor (CBF) in CV-1 and COS-7 cells, as judged by gel shift and Southwestern analyses. Similar results were obtained in human fibroblasts expressing a conditional SV40-LT. The SV40-LT inducible CBF

appears to be novel and differs from the CBF that activates heat shock protein 70 gene expression.

L18 ANSWER 20 OF 26 HCAPLUS COPYRIGHT 2000 ACS
AN 1996:355127 HCAPLUS
DN 125:31173
TI Inactivation of multiple tumor-suppressor genes involved in negative regulation of the cell cycle, MTS1/p16INK4A/CDKN2, MTS2/p15INK4B, p53, and Rb genes in primary lymphoid malignancies
AU Hangaishi, Akira; Ogawa, Seishi; Imamura, Nobutaka; Miyawaki, Shuichi; Miura, Yasusada; Uike, Naokuni; Shimazaki, Chihiro; Emi, Nobuhiko; Takeyama, Kunihiko; et al.
CS Faculty of Medicine, University of Tokyo, Tokyo, 113, Japan
SO Blood (1996), 87(12), 4949-4958
CODEN: BLOOAW; ISSN: 0006-4971
DT Journal
LA English
AB It is now evident that the cell cycle machinery has a variety of elements neg. regulating cell cycle progression. However, among these neg. regulators in cell cycle control, only 4 have been shown to be consistently involved in the development of human cancers as **tumor suppressors**: Rb (**Retinoblastoma** susceptibility **protein**), p53, and two recently identified cyclin-dependent kinase inhibitors, p16INK4A/MTS1 and p15INK4B/MTS2. Because there are functional interrelations among these neg. regulators in the cell cycle machinery, it is particularly interesting to investigate the multiplicity of inactivations of these tumor suppressors in human cancers, including leukemias/lymphomas. To address this point, the authors examd. inactivations of these four genes in primary lymphoid malignancies by Southern blot and polymerase chain reaction-single-strand conformation polymorphism analyses. The authors also analyzed Rb protein expression by Western blot anal. The p16INK4A and p15INK4B genes were homozygously **deleted** in 45 and 42 of 230 lymphoid tumor specimens, resp. Inactivations of the Rb and p53 genes were 27 of 91 and 9 of 173 specimens, resp. Forty-one (45.1%) of 91 samples examd. for inactivations of all four tumor suppressors had one or more abnormalities of these four tumor-suppressor genes, indicating that dysregulation of cell cycle control is important for tumor development. Statistical anal. of interrelations among impairments of these four genes indicated that inactivations of the individual tumor-suppressor genes might occur almost independently. In some patients, disruptions of multiple tumor-suppressor genes occurred; 4 cases with p16INK4A, p15INK4B, and Rb inactivations; 2 cases with p16INK4A, p15iNK4B, and p53 inactivations; and 1 case with Rb and p53 inactivations. It is suggested that disruptions of multiple tumor suppressors in a tumor cell confer an addnl. growth advantage on the tumor.

L18 ANSWER 21 OF 26 HCAPLUS COPYRIGHT 2000 ACS
AN 1996:314940 HCAPLUS
DN 125:2856
TI Inhibition of E2F activity by the cyclin-dependent protein kinase inhibitor p21 in cells expressing or lacking a functional retinoblastoma protein
AU Dimri, Goberdhan P.; Nakanishi, Makoto; Desprez, Pierre-Yves; Smith, James R.; Campisi, Judith
CS Dep. Cancer Biol., Univ. California, Berkeley, CA, 94720, USA
SO Mol. Cell. Biol. (1996), 16(6), 2987-2997
CODEN: MCEBD4; ISSN: 0270-7306
DT Journal
LA English
AB P21Sdi1/WAF1/Cip1 inhibits cyclin-dependent protein kinases and cell proliferation. P21 is presumed to inhibit growth by preventing the phosphorylation of growth-regulatory **proteins**, including the **retinoblastoma tumor suppressor protein** (pRb). The ultimate effector(s) of p21 growth inhibition, however, is largely a matter of conjecture. We show that p21 inhibits the activity of E2F, an essential growth-stimulatory transcription factor that is neg. regulated by unphosphorylated pRb. P21 suppressed the activity of E2F-responsive promoters (dihydrofolate reductase and cdc2), but E2F-unresponsive promoters (c-fos and simian virus 40 early) were

unaffected. Moreover, the simian virus 40 early promoter was rendered p21 suppressible by introducing wild-type, but not mutant, E2F binding sites; p21 suppressed a wild-type, but not mutant, E2F-1 promoter via its autoregulatory E2F binding site; p21 **deletion** mutants showed good agreement in their abilities to inhibit E2F transactivation and DNA synthesis; and E2F-1 (which binds pRb), but not E2F-4 (which does not), reversed both inhibitory effects of p21. Despite the central role for pRb in regulating E2F, p21 suppressed growth and E2F activity in cells lacking a functional pRb. Moreover, p21 protein (wild type but not mutant) specifically disrupted in E2F-cyclin-dependent protein kinase 2-p107 DNA binding complex in nuclear exts. of proliferating cells, whether or not they expressed normal pRb. Thus, E2F is a crit. target and ultimate effector of p21 action, and pRb is not essential for the inhibition of growth or E2F-dependent transcription.

L18 ANSWER 22 OF 26 HCAPLUS COPYRIGHT 2000 ACS
AN 1996:242275 HCAPLUS
DN 124:282478
TI The interferon-inducible growth-inhibitory p202 protein: DNA binding properties and identification of a DNA binding domain
AU Choubey, Divaker; Gutterman, Jordan U.
CS Dep. Molecular Oncology, The Univ. Texas M. D. Anderson Cancer Center, Houston, TX, 77030, USA
SO Biochem. Biophys. Res. Commun. (1996), 221(2), 396-401
CODEN: BBRCA9; ISSN: 0006-291X
DT Journal
LA English
AB P202 is an interferon-inducible protein whose expression in transfected cells inhibits proliferation. P202 binds to the **retinoblastoma tumor suppressor protein** in vitro and in vivo and the transcription factors AP-1, c-Fos, and c-Jun, NK-.kappa.B p50 and p65, and inhibits the transcriptional activity of these factors in vivo. Here we report that p202 nonspecifically binds to double-stranded DNA and to single-stranded DNA in vitro. Anal. with recombinant p202 revealed that DNA binding activity is intrinsic to p202. A C-terminal **deletion** mutant of p202 exhibited DNA-binding properties, indicating that the C-terminus is dispensable for DNA binding. We also found that underphosphorylated p202 efficiently binds to DNA. Our data suggest that DNA binding activity of p202 may contribute to its functions.

L18 ANSWER 23 OF 26 HCAPLUS COPYRIGHT 2000 ACS
AN 1995:618119 HCAPLUS
DN 123:2778
TI Modification of Retinoblastoma and P53 yielding permanent active states for use in gene therapy involving pathological cell proliferative diseases
IN Fung, Yuen Kai
PA Research Development Foundation, USA
SO PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9506661	A1	19950309	WO 1994-US9861	19940901
	W: AU, CA, CN, FI, JP, KR, NO, NZ, RU, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	ZA 9406595	A	19960228	ZA 1994-6595	19940830
	CA 2170605	AA	19950309	CA 1994-2170605	19940901
	AU 9476426	A1	19950322	AU 1994-76426	19940901
	AU 692793	B2	19980618		
	EP 716660	A1	19960619	EP 1994-926655	19940901
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	CN 1133595	A	19961016	CN 1994-193949	19940901
	JP 09502183	T2	19970304	JP 1994-508257	19940901
PRAI	US 1993-116943	19930903			
	WO 1994-US9861	19940901			

AB Retinoblastoma and P53 proteins were **modified** such that, when expressed, are in an active conformation, and require no further **modification** for activity. Homol. domains of P53 and

retinoblastoma proteins were identified that dets. the conformations, and thereby the activity of these proteins. By this permanent retention of P53 and **retinoblastoma tumor suppressor proteins** in their active state, cell proliferation is actively suppressed. These forms of tumor suppressor proteins may be very useful in gene therapy relating to treatment of focal cell and pathol. cell proliferative diseases.

L18 ANSWER 24 OF 26 HCAPLUS COPYRIGHT 2000 ACS
AN 1995:229994 HCAPLUS
DN 122:6845
TI A mutational analysis of the amino terminal domain of the human papillomavirus type 16 E7 oncoprotein
AU Brokaw, Jane L.; Yee, Carole L.; Munger, Karl
CS Lab. of Tumor Virus Biology, National Institutes of Health, Bethesda, MD, 20892, USA
SO Virology (1994), 205(2), 603-7
CODEN: VIRLAX; ISSN: 0042-6822
DT Journal
LA English
AB The human papillomavirus type 16 (HPV-16) E7 oncoprotein shares structural and functional similarity with the adenovirus (Ad) E1A protein and the SV40 large tumor antigen (TAg). Like these other DNA tumor virus oncoproteins, HPV-16 E7 interacts with "pocket proteins," a family of host cellular **proteins** that include the **retinoblastoma tumor suppressor protein** and can cooperate with the ras oncogene to transform primary rodent cells. Mutational analyses have indicated that amino acid sequences outside of the pRB binding region are also important for the cellular transformation property of HPV-16 E7. These sequences include an amino terminal domain of the E7 protein that is similar to a portion of conserved region 1 of Ad E1A. In this study it is shown that the homologous amino acid sequences in Ad E1A and SV40 TAg are functionally interchangeable with the amino terminal HPV-16 E7 domain in transformation assays. **Deletion** anal. across the amino terminus of HPV-16 E7 indicated that the overall integrity of the entire CR1 homol. domain is important for the biol. activity of the HPV E7 oncoprotein.

L18 ANSWER 25 OF 26 HCAPLUS COPYRIGHT 2000 ACS
AN 1993:492576 HCAPLUS
DN 119:92576
TI EBNA-5, an Epstein-Barr virus-encoded nuclear antigen, binds to the retinoblastoma and p53 proteins
AU Szekely, Laszlo; Selivanova, Galina; Magnusson, Kristinn P.; Klein, George; Wiman, Klas G.
CS Dep. Tumor Biol., Karolinska Inst., Stockholmd, S-104 01, Swed.
SO Proc. Natl. Acad. Sci. U. S. A. (1993), 90(12), 5455-9
CODEN: PNASA6; ISSN: 0027-8424
DT Journal
LA English
AB Epstein-Barr virus (EBV) immortalized human lymphoblastoid cell lines express 6 virally encoded nuclear proteins, designated EBV nuclear antigens 1-6 (EBNA-1-6). The authors show that the EBNA-5 protein (alternatively designated EBNA-LP) that is required for B-cell transformation can form a mol. complex with the **retinoblastoma** (RB) and p53 **tumor suppressor proteins**. Using EBNA-5 **deletion** mutants, the authors have found that a 66-amino acid-long peptide, encoded by the W repeat of the EBV genome, is sufficient for binding. Point mutations of RB and p53 that inhibit their complexing with other DNA viral oncoproteins do not affect their binding to EBNA-5. P53 competes with RB for EBNA-5 binding. These data suggest that the mechanisms involved in EBV transformation may include impairment of RB and p53 function.

L18 ANSWER 26 OF 26 HCAPLUS COPYRIGHT 2000 ACS
AN 1993:182888 HCAPLUS
DN 118:182888
TI Inhibition of histone H1 kinase expression, retinoblastoma protein phosphorylation, and cell proliferation by the phosphatase inhibitor okadaic acid

AU Schonthal, Axel; Feramisco, James R.
CS Cancer Cent., Univ. California, San Diego, La Jolla, CA, 92093-0636, USA
SO Oncogene (1993), 8(2), 433-41
CODEN: ONCNES; ISSN: 0950-9232
DT Journal
LA English
AB Phosphorylation events are major regulatory mechanisms of signal transduction pathways that regulate gene expression and cell growth. To study the potential involvement of serine-threonine specific phosphatases in these processes, the authors used okadaic acid (OA), an inhibitor of type 1 and type 2A protein phosphatases. Here, the authors present evidence that OA arrests cells at defined points in the cell cycle. Concomitantly, expression and assocd. histone H1 kinase activity of cdc2 and cyclin A, two cell cycle regulatory proteins, are repressed by this agent. Furthermore, phosphorylation of the **tumor suppressor protein retinoblastoma**, an event thought to be necessary in order to permit cells to proliferate, is inhibited when OA is present. These effects are fully reversible, since **removal** of OA restores cdc2 and cyclin A expression as well as histone H1 kinase activity, and the cells resume growth. Since cdc2 and cyclin A have previously been shown to be absolutely required for cell cycle progression, it is likely that blockage of synthesis of these components contributes to the cytostatic effects of OA. Furthermore, these results suggest a pos. role for OA sensitive protein phosphatases in the regulation of expression of these cell cycle regulatory proteins.

=> d bib abs 125 1-52

L25 ANSWER 1 OF 52 USPATFULL
AN 1999:124734 USPATFULL
TI DNA sequence encoding a tumor suppressor gene
IN Garkavtsev, Igor, Calgary, Canada
Riabowol, Karl, Calgary, Canada
PA University Technologies International Inc., Calgary, Canada (non-U.S. corporation)
PI US 5965398 19991012
AI US 1999-258257 19990226 (9)
RLI Continuation of Ser. No. US 1995-569721, filed on 8 Dec 1995
DT Utility
EXNAM Primary Examiner: Degen, Nancy; Assistant Examiner: McGarry, Sean
LREP Burns, Doane, Swecker & Mathis,L.L.P.
CLMN Number of Claims: 4
ECL Exemplary Claim: 1
DRWN 4 Drawing Figure(s); 5 Drawing Page(s)
LN.CNT 1035
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides novel tumor suppressor genes, methods for making and using these and related tumor suppressor genes and proteins and peptides, and nucleic acids encoding these and related tumor suppressor proteins and peptides.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L25 ANSWER 2 OF 52 USPATFULL
AN 1999:106321 USPATFULL
TI Modulators of BRCA1 activity
IN Rubinfeld, Bonnee, Danville, CA, United States
Polakis, Paul G., Mill Valley, CA, United States
Lingenfelter, Carol, Oakland, CA, United States
Vuong, Terilyn T., Oakland, CA, United States
PA Onyx Pharmaceuticals, Inc., Richmond, CA, United States (U.S. corporation)
PI US 5948643 19990907
AI US 1997-968751 19970813 (8)
DT Utility
EXNAM Primary Examiner: Hutzell, Paula K.; Assistant Examiner: Sun-Hoffman, Lin
LREP Giotta, Gregory
CLMN Number of Claims: 7
ECL Exemplary Claim: 1
DRWN 5 Drawing Figure(s); 7 Drawing Page(s)
LN.CNT 2263
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compositions of matter consisting of a family of related nucleotide sequences that encode proteins, termed BRCA1 Modulator Proteins, that bind to the tumor suppressor gene product BRCA1, and methods of using the nucleotide sequences and the proteins encoded thereby, to diagnose and/or treat disease where the BRCA1 Modulator Proteins have an apparent molecular weight of 45-97 kdaltons and are characterized by having at least one leucine zipper domain, and optionally a zinc finger domain.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L25 ANSWER 3 OF 52 USPATFULL
AN 1999:88789 USPATFULL
TI Recombinant adenoviral vector and methods of use
IN Gregory, Richard J., Carlsbad, CA, United States
Wills, Ken N., Encinitas, CA, United States
Maneval, Daniel C., San Diego, CA, United States
PA Canji Inc., San Diego, CA, United States (U.S. corporation)
PI US 5932210 19990803
AI US 1997-959638 19971028 (8)
RLI Continuation of Ser. No. US 1994-328673, filed on 25 Oct 1994 which is a continuation-in-part of Ser. No. US 1994-246006, filed on 19 May 1994, now abandoned which is a continuation-in-part of Ser. No. US

1993-142669, filed on 25 Oct 1993, now abandoned
DT Utility
EXNAM Primary Examiner: Guzo, David
LREP Townsend and Townsend and Crew
CLMN Number of Claims: 19
ECL Exemplary Claim: 1
DRWN 23 Drawing Figure(s); 23 Drawing Page(s)
LN.CNT 2379
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides a recombinant adenovirus expression vector characterized by the partial or total **deletion** of the adenoviral protein IX DNA and having a gene encoding a foreign protein or a functional fragment or mutant thereof. Transformed host cells and a method of producing recombinant proteins and gene therapy also are included within the scope of this invention. Thus, for example, the adenoviral vector of this invention can contain a foreign gene for the expression of a protein effective in regulating the cell cycle, such as p53, Rb, or mitosin, or in inducing cell death, such as the conditional suicide gene thymidine kinase. (The latter must be used in conjunction with a thymidine kinase metabolite in order to be effective).

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L25 ANSWER 4 OF 52 USPATFULL
AN 1999:75853 USPATFULL
TI Transgenic mice having **modified** cell-cycle regulation
IN Beach, David H., Huntington Bay, NY, United States
Serrano, Manuel, Mill Neck, NY, United States
DePinho, Ronald A., Pelham Manor, NY, United States
PA Cold Spring Habor Labortary, Cold Spring Habor, NY, United States (U.S. corporation)
Albert Einstein College of Medicine of Yeshiva University, Bronx, NY, United States (U.S. corporation)
PI US 5919997 19990706
AI US 1996-627610 19960404 (8)
RLI Continuation-in-part of Ser. No. US 1996-581918, filed on 2 Jan 1996 which is a continuation-in-part of Ser. No. US 1995-497214, filed on 30 Jun 1995 which is a continuation-in-part of Ser. No. US 1994-346147, filed on 29 Nov 1994 which is a continuation-in-part of Ser. No. US 1994-306511, filed on 14 Sep 1994 which is a continuation-in-part of Ser. No. US 1994-248812, filed on 25 May 1994 which is a continuation-in-part of Ser. No. US 1994-227371, filed on 14 Apr 1994 which is a continuation-in-part of Ser. No. US 1993-154915, filed on 18 Nov 1993
DT Utility
EXNAM Primary Examiner: Crouch, Deborah; Assistant Examiner: Martin, Jill D.
LREP Foley, Hoag & Eliot, LLP; Vincent, Esq., Matthew P.; Varma, Esq., Anita
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN 3 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 2992
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to transgenic mice in which the biological function of at least one cell cycle regulatory proteins of the INK4 family is altered.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L25 ANSWER 5 OF 52 USPATFULL
AN 1999:69778 USPATFULL
TI E6 associated protein
IN Huibregtse, Jon M., Brighton, MA, United States
Scheffner, Martin, Walldorf, Germany, Federal Republic of
Howley, Peter M., Wellesley, MA, United States
PA The United States of America as represented by the Department of Health and Human Services, Washington, DC, United States (U.S. government)
PI US 5914389 19990622
AI US 1996-674030 19960701 (8)
RLI Division of Ser. No. US 1993-100692, filed on 30 Jul 1993, now patented, Pat. No. US 5532348, issued on 2 Jul 1996

DT Utility
EXNAM Primary Examiner: Kemmerer, Elizabeth C.
LREP Townsend and Townsend and Crew
CLMN Number of Claims: 4
ECL Exemplary Claim: 1
DRWN 21 Drawing Figure(s); 12 Drawing Page(s)
LN.CNT 1447
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides compositions of isolated and purified E6 Associated Protein and fragments thereof. Also provided are nucleic acid constructs encoding E6 Associated Protein. These compositions may be employed to identify compounds which inhibit binding of high risk HPV E6 to p53. The compositions of the present invention may also be used in methods to detect the presence of high risk HPV in biological samples.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L25 ANSWER 6 OF 52 MEDLINE
AN 2000036560 MEDLINE
DN 20036560
TI Activation of the cyclin D1 gene by the E1A-associated protein p300 through AP-1 inhibits cellular apoptosis.
AU Albanese C; D'Amico M; Reutens A T; Fu M; Watanabe G; Lee R J; Kitsis R N; Henglein B; Avantaggiati M; Somasundaram K; Thimmapaya B; Pestell R G
CS Albert Einstein Cancer Center, Albert Einstein College of Medicine, Bronx, New York 10461, USA.
NC R29CA70896-01 (NCI)
RO1CA75503 (NCI)
5-P30-CA13330-26 (NCI)
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1999 Nov 26) 274 (48) 34186-95.
Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 200003
EW 20000301
AB The adenovirus E1A protein interferes with regulators of apoptosis and growth by physically interacting with cell cycle regulatory **proteins** including the **retinoblastoma tumor suppressor protein** and the coactivator proteins p300/CBP (where CBP is the CREB-binding protein). The p300/CBP proteins occupy a pivotal role in regulating mitogenic signaling and apoptosis. The mechanisms by which cell cycle control genes are directly regulated by p300 remain to be determined. The cyclin D1 gene, which is overexpressed in many different tumor types, encodes a regulatory subunit of a holoenzyme that phosphorylates and inactivates PRB. In the present study E1A12S inhibited the cyclin D1 promoter via the amino-terminal p300/CBP binding domain in human choriocarcinoma JEG-3 cells. p300 induced cyclin D1 protein abundance, and p300, but not CBP, induced the cyclin D1 promoter. cyclin D1 or p300 overexpression inhibited apoptosis in JEG-3 cells. The CH3 region of p300, which was required for induction of cyclin D1, was also required for the inhibition of apoptosis. p300 activated the cyclin D1 promoter through an activator protein-1 (AP-1) site at -954 and was identified within a DNA-bound complex with c-Jun at the AP-1 site. Apoptosis rates of embryonic fibroblasts derived from mice homozygously **deleted** of the cyclin D1 gene (cyclin D1(-/-)) were increased compared with wild type control on several distinct matrices. p300 inhibited apoptosis in cyclin D1(+/+) fibroblasts but increased apoptosis in cyclin D1(-/-) cells. The anti-apoptotic function of cyclin D1, demonstrated by sub-G(1) analysis and annexin V staining, may contribute to its cellular transforming and cooperative oncogenic properties.

L25 ANSWER 7 OF 52 MEDLINE
AN 2000079603 MEDLINE
DN 20079603
TI Human cells compromised for p53 function exhibit defective global and transcription-coupled nucleotide excision repair, whereas cells compromised for pRb function are defective only in global repair.
AU Therrien J P; Drouin R; Baril C; Drobetsky E A

CS Division of Pathology, Department of Medical Biology, Faculty of Medicine, Laval University, Quebec, Canada.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1999 Dec 21) 96 (26) 15038-43.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 200003
EW 20000305
AB After exposure to DNA-damaging agents, the p53 tumor suppressor protects against neoplastic transformation by inducing growth arrest and apoptosis. A series of investigations has also demonstrated that, in UV-exposed cells, p53 regulates the **removal** of DNA photoproducts from the genome overall (global nucleotide excision repair), but does not participate in an overlapping pathway that **removes** damage specifically from the transcribed strand of active genes (transcription-coupled nucleotide excision repair). Here, the highly sensitive ligation-mediated PCR was employed to quantify, at nucleotide resolution, the repair of UVB-induced cyclobutane pyrimidine dimers (CPDs) in genetically p53-deficient Li-Fraumeni skin fibroblasts, as well as in human lung fibroblasts expressing the human papillomavirus (HPV) E6 oncoprotein that functionally inactivates p53. Lung fibroblasts expressing the HPV E7 gene product, which similarly inactivates the **retinoblastoma tumor-suppressor protein** (pRb), were also investigated. pRb acts downstream of p53 to mediate G(1) arrest, but has no demonstrated role in DNA repair. Relative to normal cells, HPV E6-expressing lung fibroblasts and Li-Fraumeni skin fibroblasts each manifested defective CPD repair along both the transcribed and nontranscribed strands of the p53 and/or c-jun loci. HPV E7-expressing lung fibroblasts also exhibited reduced CPD **removal**, but only along the nontranscribed strand. Our results provide striking evidence that transcription-coupled repair, in addition to global repair, are p53-dependent in UV-exposed human fibroblasts. Moreover, the observed DNA-repair defect in HPV E7-expressing cells reveals a function for this oncoprotein in HPV-mediated carcinogenesis, and may suggest a role for pRb in global nucleotide excision repair.

L25 ANSWER 8 OF 52 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1999:468700 BIOSIS
DN PREV199900468700
TI Repression of Epstein-Barr virus EBNA-1 gene transcription by pRb during restricted latency.
AU Ruf, Ingrid K.; Sample, Jeffery (1)
CS (1) Department of Virology and Molecular Biology, St. Jude Children's Research Hospital, 332 N. Lauderdale, Memphis, TN, 38105 USA
SO Journal of Virology, (Oct., 1999) Vol. 73, No. 10, pp. 7943-7951.
ISSN: 0022-538X.
DT Article
LA English
SL English
AB During the restricted programs of Epstein-Barr virus (EBV) latency in EBV-associated tumors and a subpopulation of latently infected B cells in healthy EBV carriers, transcription of the EBV nuclear antigen 1 (EBNA-1) gene is mediated by the promoter Qp. Previously, two noncanonical E2F binding sites were identified within Qp. The role of E2F in the regulation of Qp, however, has been controversial and is undefined. Here we demonstrate that an E2F factor(s) within Burkitt lymphoma (BL) cells binds to a G/C-rich element (GGCG (C/G)) within the previously identified binding sites in Qp and prototypical E2F response elements. Furthermore, Qp-driven reporter gene expression could be efficiently repressed through either E2F binding site by the tumor suppressor pRb, a potent transcriptional repressor targeted to promoters during G0 and the early G1 phase of the cell cycle via its interaction with E2F; a mutant pRb (pRb706) lacking E2F binding capability was unable to repress Qp. However, we did not observe cell cycle variation in the expression of either EBNA-1 mRNA or protein in exponentially growing BL cells, consistent with previous predictions that Qp is constitutively active in these cells and with the extremely long t1/2 of EBNA-1. By contrast, within G0/G1 in

growth-arrested BL cells, EBNA-1 mRNA levels were twofold lower than in S phase, similar to the two- to eightfold differences in cell cycle expression of some cyclin mRNAs. Thus, although regulation of Qp is coupled to the cell cycle, this clearly has no impact on the level of EBNA-1 expressed in proliferating cells. We conclude, therefore, that the most important contribution of E2F to the regulation of Qp is to direct the pRb-mediated suppression of EBNA-1 expression within resting B cells, the principal reservoir of latent EBV. This would provide a means to restrict unneeded and potentially **deleterious** expression of EBNA-1 in a nonproliferating cell and to coordinate the activation of EBNA-1 expression necessary for EBV genome replication and maintenance upon reentry of the cell cycle in response to proliferative signals.

L25 ANSWER 9 OF 52 MEDLINE
AN 1999421947 MEDLINE
DN 99421947
TI RBP1 recruits both histone deacetylase-dependent and -independent repression activities to retinoblastoma family proteins.
AU Lai A; Lee J M; Yang W M; DeCaprio J A; Kaelin W G Jr; Seto E; Branton P E
CS Departments of Biochemistry, McGill University, Montreal, Quebec, Canada H3G 1Y6.
SO MOLECULAR AND CELLULAR BIOLOGY, (1999 Oct) 19 (10) 6632-41.
Journal code: NGY. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200004
EW 20000401
AB **Retinoblastoma** (RB) **tumor suppressor** family **proteins** block cell proliferation in part by repressing certain E2F-specific promoters. Both histone deacetylase (HDAC)-dependent and -independent repression activities are associated with the RB "pocket." The mechanism by which these two repression functions occupy the pocket is unknown. A known RB-binding protein, RBP1, was previously found by our group to be an active corepressor which, if overexpressed, represses E2F-mediated transcription via its association with the pocket. We show here that RBP1 contains two repression domains, one of which binds all three known HDACs and represses them in an HDAC-dependent manner while the other domain functions independently of the HDACs. Thus, RB family members repress transcription by recruiting RBP1 to the pocket. RBP1, in turn, serves as a bridging molecule to recruit HDACs and, in addition, provides a second HDAC-independent repression function.

L25 ANSWER 10 OF 52 MEDLINE DUPLICATE 1
AN 1999218299 MEDLINE
DN 99218299
TI Thyroid hormone, T3-dependent phosphorylation and translocation of Trip230 from the Golgi complex to the nucleus.
AU Chen Y; Chen P L; Chen C F; Sharp Z D; Lee W H
CS Department of Molecular Medicine and Institute of Biotechnology, University of Texas Health Science Center at San Antonio, San Antonio, TX 78245-3207, USA.
NC EY05758 (NEI)
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1999 Apr 13) 96 (8) 4443-8.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199907
EW 19990704
AB Trip230 is a novel coactivator of the thyroid hormone receptor that is negatively regulated by the **retinoblastoma tumor-suppressor protein**. In an examination of its subcellular distribution, Trip230 localized predominantly to the vicinity of the Golgi instead of the nucleus, as other nuclear hormone receptor coactivators. Using a series of **deletion** mutants, a critical region identified for Golgi area targeting coincided with a previously defined thyroid

hormone receptor-binding domain of Trip230. During cell cycle progression, the expression level of Trip230 is constant and a significant portion is imported into the nucleus at S phase. Within an hour of treating cells with T3, Trip230 immunofluorescence transiently colocalized with TR in prominent subnuclear structures. T3-dependent nuclear import of Trip230 does not require new protein synthesis. Coincident with T3 treatment and nuclear import, newly phosphorylated residue(s) appeared in Trip230, suggesting that phosphorylation may be involved in its nuclear import. These findings provided a novel mechanism for the regulation of nuclear hormone transcription factors by hormone-responsive phosphorylation and nuclear import of cytoplasmically located coactivators.

L25 ANSWER 11 OF 52 MEDLINE DUPLICATE 2
AN 1999173997 MEDLINE
DN 99173997
TI The retinoblastoma protein alters the phosphorylation state of polyomavirus large T antigen in murine cell extracts and inhibits polyomavirus origin DNA replication.
AU Reynisdottir I; Bhattacharyya S; Zhang D; Prives C
CS Department of Biological Sciences, Columbia University, New York, New York 10027, USA.
NC CA26905 (NCI)
SO JOURNAL OF VIROLOGY, (1999 Apr) 73 (4) 3004-13.
Journal code: KCV. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199907
EW 19990702
AB The **retinoblastoma tumor suppressor protein** (pRb) can associate with the transforming proteins of several DNA tumor viruses, including the large T antigen encoded by polyomavirus (Py T Ag). Although pRb function is critical for regulating progression from G1 to S phase, a role for pRb in S phase has not been demonstrated or excluded. To identify a potential effect of pRb on DNA replication, pRb protein was added to reaction mixtures containing Py T Ag, Py origin-containing DNA (Py ori-DNA), and murine FM3A cell extracts. We found that pRb strongly represses Py ori-DNA replication in vitro. Unexpectedly, however, this inhibition only partially depends on the interaction of pRb with Py T Ag, since a mutant Py T Ag (dl141) lacking the pRb interaction region was also significantly inhibited by pRb. This result suggests that pRb interferes with or alters one or more components of the murine cell replication extract. Furthermore, the ability of Py T Ag to be phosphorylated in such extracts is markedly reduced in the presence of pRb. Since cyclin-dependent kinase (CDK) phosphorylation of Py T Ag is required for its replication function, we hypothesize that pRb interferes with this phosphorylation event. Indeed, the S-phase CDK complex (cyclin A-CDK2), which phosphorylates both pRb and Py T Ag, alleviates inhibition caused by pRb. Moreover, hyperphosphorylated pRb is incapable of inhibiting replication of Py ori-DNA in vitro. We propose a new requirement for maintaining pRb phosphorylation in S phase, namely, to prevent **deleterious** effects on the cellular replication machinery.

L25 ANSWER 12 OF 52 MEDLINE DUPLICATE 3
AN 1999403006 MEDLINE
DN 99403006
TI A genetic screen for **modifiers** of E2F in Drosophila melanogaster.
AU Staehling-Hampton K; Ciampa P J; Brook A; Dyson N
CS Massachusetts General Hospital Cancer Center, Charlestown, Massachusetts 02129, USA.
NC GM-53203 (NIGMS)
SO GENETICS, (1999 Sep) 153 (1) 275-87.
Journal code: FNH. ISSN: 0016-6731.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals

EM 200001
EW 20000104
AB The activity of the E2F transcription factor is regulated in part by pRB, the **protein** product of the **retinoblastoma tumor suppressor** gene. Studies of tumor cells show that the p16(ink4a)/cdk4/cyclin D/pRB pathway is mutated in most forms of cancer, suggesting that the deregulation of E2F, and hence the cell cycle, is a common event in tumorigenesis. Extragenic mutations that enhance or suppress E2F activity are likely to alter cell-cycle control and may play a role in tumorigenesis. We used an E2F overexpression phenotype in the Drosophila eye to screen for **modifiers** of E2F activity. Coexpression of dE2F and its heterodimeric partner dDP in the fly eye induces S phases and cell death. We isolated 33 enhancer mutations of this phenotype by EMS and X-ray mutagenesis and by screening a deficiency library collection. The majority of these mutations sorted into six complementation groups, five of which have been identified as alleles of brahma (brm), moira (mor) osa, pointed (pnt), and polycephalon (poc). osa, brm, and mor encode proteins with homology to SWI1, SWI2, and SWI3, respectively, suggesting that the activity of a SWI/SNF chromatin-remodeling complex has an important impact on E2F-dependent phenotypes. Mutations in poc also suppress phenotypes caused by p21(CIP1) expression, indicating an important role for polycephalon in cell-cycle control.

L25 ANSWER 13 OF 52 MEDLINE DUPLICATE 4
AN 1999177928 MEDLINE
DN 99177928
TI Mechanism of transcriptional repression of E2F by the **retinoblastoma tumor suppressor protein**.
AU Ross J F; Liu X; Dynlacht B D
CS Department of Molecular and Cellular Biology, Cambridge, Massachusetts 02138, USA.
NC 1 R01 CA77245-01 (NCI)
SO MOLECULAR CELL, (1999 Feb) 3 (2) 195-205.
Journal code: C5E. ISSN: 1097-2765.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199906
EW 19990603
AB The **retinoblastoma tumor suppressor protein** (pRB) is a transcriptional repressor, critical for normal cell cycle progression. We have undertaken studies using a highly purified reconstituted in vitro transcription system to demonstrate how pRB can repress transcriptional activation mediated by the E2F transcription factor. Remarkably, E2F activation became resistant to pRB-mediated repression after the establishment of a partial (TFIIA/TFIID) preinitiation complex (PIC). DNase I footprinting studies suggest that E2F recruits TFIID to the promoter in a step that also requires TFIIA and confirm that recruitment of the PIC by E2F is blocked by pRB. These studies suggest a detailed mechanism by which E2F activates and pRB represses transcription without the requirement of histone-**modifying** enzymes.

L25 ANSWER 14 OF 52 USPATFULL
AN 1998:157173 USPATFULL
TI Polypeptides from Kaposi's sarcoma-associated herpesvirus, DNA encoding same and uses thereof
IN Chang, Yuan, New York, NY, United States
Bohenzky, Roy A., Mountian View, CA, United States
Russo, James J., New York, NY, United States
Edelman, Isidore S., New York, NY, United States
Moore, Patrick S., New York, NY, United States
PA The Trustees of Columbia University in the City of New York, New York, NY, United States (U.S. corporation)
PI US 5849564 19981215
AI US 1996-770379 19961129 (8)
DT Utility

EXNAM Primary Examiner: Myers, Carla J.
LREP White, John P.Cooper & Dunham LLP
CLMN Number of Claims: 12
ECL Exemplary Claim: 1,6,7
DRWN 29 Drawing Figure(s); 16 Drawing Page(s)
LN.CNT 6146
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides an isolated nucleic acid molecule which encodes Kaposi's Sarcoma-Associated Herpesvirus (KSHV) polypeptides. This invention provides an isolated polypeptide molecule of KSHV. This invention provides an antibody specific to the polypeptide. Antisense and triplex oligonucleotide molecules are also provided. This invention provides a vaccine for Kaposi's Sarcoma (KS). This invention provides methods of vaccination, prophylaxis, diagnosis and treatment of a subject with KS and of detecting expression of a DNA virus associated with Kaposi's sarcoma in a cell.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L25 ANSWER 15 OF 52 USPATFULL
AN 1998:118842 USPATFULL
TI Methods for the suppression of neu mediated phenotype in tumors
IN Hung, Mien-Chie, Houston, TX, United States
Yu, Di-Hua, Houston, TX, United States
Matin, Angabin, Houston, TX, United States
Zhang, Yujiao Joe, Houston, TX, United States
PA Board of Regents, The University of Texas System, Austin, TX, United States (U.S. corporation)
PI US 5814315 19980929
AI US 1995-457029 19950601 (8)
RLI Continuation of Ser. No. US 1994-276359, filed on 15 Jul 1994, now patented, Pat. No. US 5643567, issued on 1 Jul 1997 which is a continuation-in-part of Ser. No. US 1993-162406, filed on 3 Dec 1993, now patented, Pat. No. US 5641484, issued on 24 Jun 1997 which is a continuation-in-part of Ser. No. US 1993-70410, filed on 4 Jun 1993, now patented, Pat. No. US 5651964, issued on 29 Jul 1997 which is a continuation-in-part of Ser. No. US 1990-621465, filed on 4 Dec 1990, now abandoned
DT Utility
EXNAM Primary Examiner: Crouch, Deborah
LREP Arnold, White & Durkee
CLMN Number of Claims: 32
ECL Exemplary Claim: 1
DRWN 65 Drawing Figure(s); 35 Drawing Page(s)
LN.CNT 3453
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are methods and compositions for the suppression of expression of the neu oncogene, as well as suppression of neu oncogene-mediated transformation, tumorigenesis and metastasis. The method disclosed involves introduction of adenovirus early 1A gene (the E1A gene) products, or the large T antigen (the LT gene product), or both into affected cells. These products, which are preferably introduced by transfection of the E1A gene into affected cells, serve to suppress neu gene expression as measured by a reduction of p185 expression. Furthermore, the E1A gene products surprisingly serve to suppress the oncogenic phenotype, as indicated by a reduction in cell growth, growth in soft agar, as well as tumorigenic and metastatic potential in vivo. The inventors propose that E1A gene products, LT gene products or derivatives therefrom, may ultimately be employed a treatment modalities for neu-mediated cancers, such as cancers of the female genital tract and breast. The inventors also propose methods of transfecting cells with either the E1A or the LT gene products using adenoviral vectors or liposomes.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L25 ANSWER 16 OF 52 USPATFULL
AN 1998:36530 USPATFULL
TI Method and kit for evaluating human papillomavirus transformed cells
IN Munger, Karl, Brookline, MA, United States

Jones, D. Leanne, Somerville, MA, United States
PA President and Fellows of Harvard College, Cambridge, MA, United States (U.S. corporation)
Harvard University, Office of Technology Transfer, Cambridge, MA, United States (U.S. corporation)
PI US 5736318 19980407
AI US 1995-406248 19950317 (8)
DT Utility
EXNAM Primary Examiner: Knode, Marian C.; Assistant Examiner: Salimi, Ali R.
LREP Hale and Dorr LLP
CLMN Number of Claims: 1
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 789
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides methods and kits for determining the extent of interaction and/or inactivation between a cyclin/cyclin-dependent kinase inhibitor and the human papilomavirus E7 oncoprotein and thus for evaluating the proliferative state of a transformed cell. Methods for identifying compounds capable of inhibiting the interaction between a cyclin/cyclin-dependent kinase inhibitor and the human papilomavirus E7 oncoprotein, and for inhibiting growth of a human papillomavirus-associated carcinoma cell are also provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L25 ANSWER 17 OF 52 USPATFULL
AN 1998:11878 USPATFULL
TI Methods for the diagnosis of a genetic predisposition to cancer associated with variant CDK4 allele
IN Dracopoli, Nicolas, Carlsbad, CA, United States
Tucker, Margaret, Bethesda, MD, United States
Goldstein, Alisa, Rockville, MD, United States
PA Sequana Theraputics, Inc., La Jolla, CA, United States (U.S. corporation)
The United States of America, Washington, DC, United States (U.S. government)
PI US 5714329 19980203
AI US 1995-564002 19951129 (8)
DT Utility
EXNAM Primary Examiner: Houtteman, Scott W.
LREP Sherwood, PamelaBozicevic & Reed, LLP
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 675
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Protein complexes consisting of a cyclin dependent kinase CDK4 and cyclin D control passage through the G1 checkpoint of the cell cycle by phosphorylating the retinoblastoma protein. The ability of these complexes to phosphorylate RB is inhibited by a family of low molecular weight proteins, including p16, p15 and p18. Germline mutations in the p16 gene have been identified in approximately half of families with hereditary A mutation is described in CDK4 in two unrelated melanoma families that do not carry germline p16 mutations. This CDK4-R24C mutation was detected in 11/11 melanoma patients, 2/17 unaffecteds and 0/5 spouses. This mutation has a specific effect of the p16 binding domain of CDK4, but has no effect on its ability to bind cyclin D and form a functional kinase. Therefore, the germline R24C mutation in CDK4 generates a dominant oncogene that is resistant to normal physiological inhibition by p16.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L25 ANSWER 18 OF 52 USPATFULL
AN 1998:7171 USPATFULL
TI Characterization of a novel anti-p110.sup.RB monoclonal antibody
IN Shepard, H. Michael, Carlsbad, CA, United States
Wen, Shu Fen, San Diego, CA, United States
PA Canji, Inc., San Diego, CA, United States (U.S. corporation)

PI US 5710255 19980120
WO 9401467 19940120
AI US 1994-204329 19940815 (8)
WO 1992-US5866 19920714
19940815 PCT 371 date
19940815 PCT 102(e) date
DT Utility
EXNAM Primary Examiner: Feisee, Lila; Assistant Examiner: Eyler, Yvonne
LREP Townsend and Townsend and Crew LLP
CLMN Number of Claims: 2
ECL Exemplary Claim: 1
DRWN 6 Drawing Figure(s); 6 Drawing Page(s)
LN.CNT 569
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides a family of monoclonal antibodies specific for epitopes of p110.sup.RB protein present in the nucleus. These antibodies have superior properties that prove useful for the detection of p110.sup.RB or its complexes with other cellular regulatory proteins in cells and in cell lysates. This invention also provides hybridoma cell lines that produce such monoclonal antibodies and methods of using these antibodies diagnostically, prognostically and therapeutically. Further, the invention provides a method for isolating proteins associated with p110.sup.RB proteins.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L25 ANSWER 19 OF 52 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1999:17770 BIOSIS
DN PREV199900017770
TI Identification of AP-2 as a interactive target of Rb and a regulator of the G1/S control element of the hamster histone H3.2 promoter.
AU Wu, Frank; Lee, Amy S. (1)
CS (1) Dep. Biochemistry Molecular Biology, Univ. Southern Calif. Sch. Med., 1441 Eastlake Avenue, Los Angeles, CA 90033 USA
SO Nucleic Acids Research, (Nov. 1, 1998) Vol. 26, No. 21, pp. 4837-4845. ISSN: 0305-1048.
DT Article
LA English
AB Previous studies have established that a 32 bp cis-regulatory region, referred to as the H3core spanning -241 to -210 of the hamster histone H3.2 promoter, is critical for its G1/S-phase induction of transcription. Here we report that the transcription factor AP-2 is a major component of the protein complex which interacts with the H3core from hamster nuclear extracts. In search of the control mechanism(s) whereby AP-2 can mediate cell cycle regulation of the histone H3.2 promoter, we found that AP-2 can physically interact with the **retinoblastoma** (Rb) **tumor suppressor protein** in vitro, and when over-expressed, can also associate with Rb in vivo. Importantly, in contrast to the majority of Rb binding proteins, the C-terminal domain of Rb alone is sufficient for its interaction with AP-2. Using a reporter gene system linking tandem copies of the H3core to a heterologous minimal promoter, we demonstrated that over-expression of AP-2 proteins results in transactivation of the reporter gene through the H3core in a sequence-specific but orientation-independent manner. Additionally, this stimulative effect was suppressed by co-expression of Rb. Thus, AP-2, through its physical and functional interaction with Rb, may contribute to the cell cycle regulation of its target genes.

L25 ANSWER 20 OF 52 MEDLINE DUPLICATE 5
AN 1999153739 MEDLINE
DN 99153739
TI Re-expression of endogenous p16ink4a in oral squamous cell carcinoma lines by 5-aza-2'-deoxycytidine treatment induces a senescence-like state.
AU Timmermann S; Hinds P W; Munger K
CS Pathology Department and Harvard Center for Cancer Biology, Harvard Medical School, Boston, Massachusetts 02115, USA.
NC 1 PO1 DE12467-01 (NIDR)
SO ONCOGENE, (1998 Dec 31) 17 (26) 3445-53.
Journal code: ONC. ISSN: 0950-9232.
CY ENGLAND: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199905
EW 19990503
AB We have previously reported that a set of oral squamous cell carcinoma lines express specifically elevated cdk6 activity. One of the cell lines, SCC4, contains a cdk6 amplification and expresses functional p16ink4a, the other cell lines express undetectable levels of p16ink4a, despite a lack of coding-region mutations. Two of the cell lines, SCC15 and SCC40 have a hypermethylated p16ink4A promoter and a third cell line, SCC9, has a mutation in the p16ink4a promoter. Using the demethylation agent 5-aza-2'-deoxycytidine, we showed that the p16ink4a protein was re-expressed after a 5-day treatment with this chemical. One cell line, SCC15 expressed high levels of p16ink4a. In this line, cdk6 activity was decreased after 5-aza-2'deoxycytidine treatment, and the hypophosphorylated, growth **suppressive** form of the **retinoblastoma tumor suppressor protein** pRB was detected. Expression of p16ink4a persisted, even after the drug was **removed** and the cells expressed senescence-associated beta-galactosidase activity. Ectopic expression of p16ink4a with a recombinant retrovirus in this cell line also induced a similar senescence-like phenotype. Hence, it was possible to restore a functional pRB pathway in an oral squamous cell carcinoma line by inducing re-expression of endogenous p16ink4a in response to treatment with a demethylating agent.

L25 ANSWER 21 OF 52 MEDLINE DUPLICATE 6
AN 1998288804 MEDLINE
DN 98288804
TI Release of cell cycle constraints in mouse melanocytes by overexpressed mutant E2F1E132, but not by **deletion** of p16INK4A or p21WAF1/CIP1.
AU Halaban R; Cheng E; Zhang Y; Mandigo C E; Miglarese M R
CS Department of Dermatology, Yale University School of Medicine, New Haven, Connecticut 06510, USA.
SO ONCOGENE, (1998 May 14) 16 (19) 2489-501.
Journal code: ONC. ISSN: 0950-9232.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199809
EW 19980901
AB Compared to normal melanocytes, melanoma cell lines exhibit overexpression of hyperphosphorylated **retinoblastoma tumor suppressor protein** (Rb) or a marked decrease in, or lack of, expression of Rb. Hyperphosphorylation of Rb results in increased E2F-mediated transactivation of target genes and cell cycle progression. Using a combination of gene disruption and ectopic expression in growth factor-dependent mouse melanocytes, we studied the roles of E2F1 and the p16INK4A and p21WAF1/CIP1 CKIs (cyclin dependent kinase inhibitors) in the acquisition of TPA (12-O-tetradecanoyl phorbol-13-acetate)-independent growth in culture, a hallmark of melanomas. Surprisingly, melanocytes from p16INK4A- or p21WAF1/CIP1-null mice remained TPA-dependent, and disruption of p21WAF1/CIP1 accelerated cell death in the absence of this mitogen. Disruption of E2F1 had the most profound effect on melanocyte growth, resulting in a fourfold decrease in growth rate in the presence of TPA. Furthermore, enforced overexpression of the DNA-binding-defective E2F1E132 mutant conferred TPA-independence upon melanocytes and was associated with sequestration of Rb and constitutive expression of E2F1 target genes, including p21WAF1/CIP1. We conclude that neutralization of Rb by E2F1E132, but not the disruption of p16INK4A or p21WAF1/CIP1, resulted in the accumulation of free E2F and cell cycle progression. Thus, mechanisms other than the loss of p16INK4A or p21WAF1/CIP1 that activate E2F may play an important role in melanomas.

L25 ANSWER 22 OF 52 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1998:498084 BIOSIS
DN PREV199800498084

TI Histone deacetylase and the retinoblastoma protein.
AU Magnaghi-Jaulin, L. (1); Groisman, R.; Naguibneva, I.; Robin, P.; Trouche, D.; Harel-Bellan, A.
CS (1) Lab. Oncogenese, Differenciation Transduction du signal, CNRS UPR 9079, IFC-01, 94801 Villejuif France
SO Bulletin du Cancer (Paris), (July, 1998) Vol. 85, No. 7, pp. 606-607. ISSN: 0007-4551.
DT Article
LA French
SL French; English
AB The balance between cellular proliferation and differentiation is strictly controlled in the cell and the deregulation of this balance can lead to tumour formation. The tumour suppressor protein Rb plays a key role in this balance essentially by repressing progression through the cell cycle and there by it blocks the cell in G1 phase. Rb represses S phase genes through the recruitment of an enzyme which **modifies** DNA structure, the histone deacetylase HDAC1. The Rb/HDAC1 complex is a key element in the control of cell proliferation and differentiation. Moreover, this complex is likely to be a target for transforming viral proteins.

L25 ANSWER 23 OF 52 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1998:450844 BIOSIS
DN PREV199800450844
TI Immunohistochemical overexpression of p16 protein associated with intact retinoblastoma protein expression in cervical cancer and cervical intraepithelial neoplasia.
AU Sano, Takaaki (1); Oyama, Tetsunari; Kashiwabara, Kenji; Fukuda, Toshio; Nakajima, Takashi
CS (1) Second Dep. Pathol., Gunma Univ. Sch. Med., 3-39-22 Showamachi, Maebashi, Gunma 371-8511 Japan
SO Pathology International, (Aug., 1998) Vol. 48, No. 8, pp. 580-585. ISSN: 1320-5463.
DT Article
LA English
AB Both p16 and retinoblastoma (Rb) proteins are important tumor suppressors that regulate the cell cycle. The status of both proteins in invasive cervical cancer and cervical intraepithelial neoplasia (CIN) has not yet been examined. The aim of this study was to investigate the expression of p16 and Rb proteins by immunohistochemistry using 98 formalin-fixed and paraffin-embedded samples of various cervical neoplastic lesions. Strong immunoreactivity for the p16 protein was observed in both the nuclei and cytoplasm of all CIN and invasive cancer cases except several low-grade CIN lesions. Expression of Rb protein was also demonstrated in the scattered nuclei of neoplastic and normal cells in all cases investigated. The results suggest that the **deletion** or mutational inactivity of both p16 and Rb proteins may be a rare event in cervical carcinogenesis. Moreover, overexpression of the p16 protein may be a useful diagnostic marker for cervical neoplastic lesions on routine laboratory screening.

L25 ANSWER 24 OF 52 MEDLINE DUPLICATE 7
AN 1998122343 MEDLINE
DN 98122343
TI TCR antigen-induced cell death occurs from a late G1 phase cell cycle check point.
AU Lissy N A; Van Dyk L F; Becker-Hapak M; Vocero-Akbani A; Mendler J H; Dowdy S F
CS Howard Hughes Medical Institute, Department of Pathology, Washington University School of Medicine, St. Louis, Missouri 63110, USA.
SO IMMUNITY, (1998 Jan) 8 (1) 57-65.
Journal code: CCF. ISSN: 1074-7613.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199804
EW 19980404
AB **Deletion** of antigen-activated T cells after an immune response and during peripheral negative selection after strong T cell receptor

(TCR) engagement of cycling T cells occurs by an apoptotic process termed TCR antigen-induced cell death (AID). By analyzing the timing of death, cell cycle markers, BrdU-labeled S phase cells, and phase-specific centrifugally elutriated cultures from stimulated Jurkat T cells and peripheral blood lymphocytes, we found that AID occurs from a late G1 check point prior to activation of cyclin E:Cdk2 complexes. T cells stimulated to undergo AID can be rescued by effecting an early G1 block by direct transduction of p16INK4a tumor suppressor protein or by inactivation of the **retinoblastoma tumor suppressor protein** (pRb) by transduced HPV E7 protein. These results suggest that AID occurs from a late G1 death check point in a pRb-dependent fashion.

L25 ANSWER 25 OF 52 MEDLINE
AN 1998086017 MEDLINE
DN 98086017
TI Etiological involvement of oncogenic human papillomavirus in tonsillar squamous cell carcinomas lacking retinoblastoma cell cycle control.
AU Andl T; Kahn T; Pfuhl A; Nicola T; Erber R; Conradt C; Klein W; Helbig M; Dietz A; Weidauer H; Bosch F X
CS Molekularbiologisches Labor, Hals-Nasen-Ohren-Klinik, Universitat Heidelberg, Germany.
SO CANCER RESEARCH, (1998 Jan 1) 58 (1) 5-13.
Journal code: CNF. ISSN: 0008-5472.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199803
EW 19980304
AB Two hundred eight primary squamous cell carcinomas of the head and neck have been analyzed with respect to the presence of the **retinoblastoma tumor suppressor protein**, pRb. Of these, 23 tumors (11%) that preferentially localized to the tonsils revealed complete absence or dramatic reduction in the amount of pRb. Other cell cycle components, cyclin D1 and p16INK4A, which are intimately related to pRb through an autoregulatory loop, were also dramatically decreased or overexpressed, respectively, in these pRb-defective tumors. On the other hand, the majority of the pRb-defective tumors contained the wild-type p53 gene. No evidence was found for genetic defects at the Rb locus in these tumors. Very significantly, in 11 of 12 pRb-defective tonsillar tumors, but in none of 9 pRb-positive tonsillar tumors ($P < 10[-7]$), DNA of oncogenic human papillomavirus types was identified, providing a strong indication for a human papillomavirus-associated etiology of these tumors and suggesting the functional inactivation of the pRb protein by the viral E7 gene product. In comparison to all head and neck squamous cell carcinomas studied, the pRb-defective tonsillar tumors were in general more poorly differentiated ($P = 0.0059$), and they were all metastatic at the time of resection. Of particular clinical interest, despite these adverse histopathological factors, the clinical outcome for these patients was relatively favorable, strongly implying that the pRb-defective tumors responded uniformly well toward postoperative radiation therapy.

L25 ANSWER 26 OF 52 USPATFULL
AN 97:61549 USPATFULL
TI Detection of inherited and somatic mutations of APC gene in colorectal cancer of humans
IN Albertsen, Hans, Salt Lake City, UT, United States
Anand, Rakesh, Cheshire, England
Carlson, Mary, Salt Lake City, UT, United States
Groden, Joanna, Salt Lake City, UT, United States
Hedge, Philip John, Cheshire, England
Joslyn, Geoff, Salt Lake City, UT, United States
Kinzler, Kenneth, Baltimore, MD, United States
Markham, Alexander, Cheshire, England
Nakamura, Yusuke, Tokyo, Japan
Thliveris, Andrew, Salt Lake City, UT, United States
Vogelstein, Bert, Baltimore, MD, United States
White, Raymond L., Salt Lake City, UT, United States

PA The John Hopkins University, Baltimore, MD, United States (U.S. corporation)
University of Utah, Salt Lake City, UT, United States (U.S. corporation)
Japanese Foundation for Cancer Research Cancer Institute, Tokyo, Japan (non-U.S. corporation)
Zeneca Limited, Cheshire, England (non-U.S. corporation)
PI US 5648212 19970715
AI US 1994-289548 19940812 (8)
RLI Division of Ser. No. US 1991-741940, filed on 8 Aug 1991, now patented, Pat. No. US 5352775
PRAI GB 1991-962 19910116
GB 1991-963 19910116
GB 1991-974 19910116
GB 1991-975 19910116
DT Utility
EXNAM Primary Examiner: Zitomer, Stephanie W.; Assistant Examiner: Tran, Paul B.
LREP Banner & Witcoff, Ltd.
CLMN Number of Claims: 36
ECL Exemplary Claim: 1
DRWN 74 Drawing Figure(s); 72 Drawing Page(s)
LN.CNT 2430
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods are provided for assessing mutations of the APC gene in human tissues and body samples. APC mutations are found in familial adenomatous polyposis patients as well as in sporadic colorectal cancer patients. APC is expressed in most normal tissues. APC is a tumor suppressor.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L25 ANSWER 27 OF 52 USPATFULL
AN 97:56335 USPATFULL
TI Methods for the suppression of neu mediated tumors by adenoviral E1A and SV40 large T antigen
IN Hung, Mien-Chie, Houston, TX, United States
Yu, Di-Hua, Houston, TX, United States
Matin, Angahin, Houston, TX, United States
Zhang, Yujiao Joe, Houston, TX, United States
PA Board of Regents, The University of Texas System, Austin, TX, United States (U.S. corporation)
PI US 5643567 19970701
AI US 1994-276359 19940715 (8)
RLI Continuation-in-part of Ser. No. US 1993-162406, filed on 3 Dec 1993 which is a continuation-in-part of Ser. No. US 1993-70410, filed on 4 Jun 1993 which is a continuation-in-part of Ser. No. US 1990-621465, filed on 4 Dec 1990, now abandoned
DT Utility
EXNAM Primary Examiner: Crouch, Deborah
LREP Arnold, White & Durkee
CLMN Number of Claims: 22
ECL Exemplary Claim: 1
DRWN 69 Drawing Figure(s); 40 Drawing Page(s)
LN.CNT 3385
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are methods and compositions for the suppression of expression of the neu oncogene, as well as suppression of neu oncogene-mediated transformation, tumorigenesis and metastasis. The method disclosed involves introduction of adenovirus early 1A gene (the E1A gene) products, or the large T antigen (the LT gene product), or both into affected cells. These products, which are preferably introduced by transfection of the E1A gene into affected cells, serve to suppress neu gene expression as measured by a reduction of p185 expression. Furthermore, the E1A gene products surprisingly serve to suppress the oncogenic phenotype, as indicated by a reduction in cell growth, growth in soft agar, as well as tumorigenic and metastatic potential in vivo. The inventors propose that E1A gene products, LT gene products or derivatives therefrom, may ultimately be employed a treatment modalities for neu-mediated cancers, such as cancers of the female genital tract and breast. The inventors also propose methods of transfecting cells

with either the E1A or the LT gene products using adenoviral vectors or liposomes.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L25 ANSWER 28 OF 52 USPATFULL
AN 97:53936 USPATFULL
TI Methods for the suppression of neu mediated tumors by adenoviral E1A and SV40 large T antigen
IN Hung, Mien-Chie, Houston, TX, United States
Yu, Di-Hua, Houston, TX, United States
Matin, Angabin, Houston, TX, United States
PA Board of Regents, The University of Texas System, Austin, TX, United States (U.S. corporation)
PI US 5641484 19970624
AI US 1993-162406 19931203 (8)
RLI Continuation-in-part of Ser. No. US 1993-70410, filed on 4 Jun 1993 which is a continuation-in-part of Ser. No. US 1990-621465, filed on 4 Dec 1990, now abandoned
DT Utility
EXNAM Primary Examiner: Crouch, Deborah
LREP Arnold, White & Durkee
CLMN Number of Claims: 43
ECL Exemplary Claim: 1
DRWN 54 Drawing Figure(s); 31 Drawing Page(s)
LN.CNT 3192
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are methods and compositions for the suppression of expression of the neu oncogene, as well as suppression of neu oncogene-mediated transformation, tumorigenesis and metastasis. The method disclosed involves introduction of adenovirus early 1A gene (the E1A gene) products, so to large T antigen (the LT gene product), or both into affected cells. These products, which are preferably introduced by transfection of the E1A gene into affected cells, serve to suppress neu gene expression as measured by a reduction of p185 expression. Furthermore, the E1A gene products surprisingly serve to suppress the oncogenic phenotype, as indicated by a reduction in cell growth, growth in soft agar, as well as tumorigenic and metastatic potential in vivo. The inventors propose that E1A gene products, LT gene products or derivatives therefrom, may ultimately be employed a treatment modalities for neu-mediated cancers, such as cancers of the female genital tract and breast. The inventors also propose methods of transfecting cells with either the E1A or the LT gene products using liposomes.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L25 ANSWER 29 OF 52 USPATFULL
AN 97:36291 USPATFULL
TI Peptide inhibitors of the p33.sup.cdk2 and p34.sup.cdc2 cell cycle regulatory kinases and human papillomavirus E7 oncoprotein
IN Webster, Kevin R., Newton, PA, United States
Coleman, Kevin G., Hopewell, NJ, United States
PA Bristol-Myers Squibb Company, New York, NY, United States (U.S. corporation)
PI US 5625031 19970429
AI US 1994-193977 19940208 (8)
DT Utility
EXNAM Primary Examiner: Wax, Robert A.; Assistant Examiner: Grimes, Eric
LREP Reed & Robins
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN 6 Drawing Figure(s); 4 Drawing Page(s)
LN.CNT 1175
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Novel peptide and peptide mimetic ligands which act as inhibitors of p34.sup.cdc2 kinase, p33.sup.cdk2 kinase and human papillomavirus transforming protein E7 (HPV E7) are disclosed. The inhibitors are derived from the binding domains of a **retinoblastoma tumor suppressor protein** (Rb), p107 and a cyclin.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L25 ANSWER 30 OF 52 MEDLINE
AN 1998043708 MEDLINE
DN 98043708
TI The human papillomavirus E7 oncoprotein functionally interacts with the S4 subunit of the 26 S proteasome.
AU Berezutskaya E; Bagchi S
CS Department of Biochemistry, University of Illinois at Chicago, Chicago, Illinois 60612, USA.
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1997 Nov 28) 272 (48) 30135-40.
Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199802
EW 19980204
AB Human papillomaviruses (HPV) have been etiologically linked to human cervical cancer. More than 90% of cervical cancer tissues express two HPV-encoded oncoproteins E6 and E7. Both E6 and E7 proteins possess transformation activity. and together they cooperate to transform primary human keratinocytes, fibroblasts. and epithelial cells. The transforming activity of E7 is associated with its ability to bind the **retinoblastoma tumor suppressor protein** (Rb). However, the carboxyl-terminal mutants of E7 are also defective for transformation, suggesting that other cellular targets for E7 might exist. We screened a human placenta cDNA library by yeast two-hybrid assay using HPV 16 E7 as a bait and identified the subunit 4 (S4) ATPase of the 26 S proteasome as a novel E7-binding protein. E7 binds to S4 through the carboxyl-terminal zinc binding motif, and the binding is independent of E7 sequences involved in binding to Rb. The interaction between S4 and E7 can be easily detected by in vitro protein binding assays. Moreover, we found that E7 increases the ATPase activity of S4. A recent study has shown that, in epithelial cells, E7 degrades Rb through the 26 S proteasome pathway. We hypothesize that E7 might target Rb for degradation by 26 S proteasome through its interaction with the subunit 4 of the proteasome.

L25 ANSWER 31 OF 52 MEDLINE DUPLICATE 8
AN 97366650 MEDLINE
DN 97366650
TI Both conserved region 1 (CR1) and CR2 of the human papillomavirus type 16 E7 oncogene are required for induction of epidermal hyperplasia and tumor formation in transgenic mice.
AU Gulliver G A; Herber R L; Liem A; Lambert P F
CS McArdle Laboratory for Cancer Research, University of Wisconsin Medical School, Madison 53706, USA.
NC CA07175 (NCI)
CA09075 (NCI)
CA22443 (NCI)
+
SO JOURNAL OF VIROLOGY, (1997 Aug) 71 (8) 5905-14.
Journal code: KCV. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Cancer Journals; Priority Journals
EM 199710
AB High-risk human papillomavirus type 16 (HPV-16) and HPV-18 are associated with the majority of human cervical carcinomas, and two viral genes, HPV E6 and E7, are commonly found to be expressed in these cancers. The presence of HPV-16 E7 is sufficient to induce epidermal hyperplasia and epithelial tumors in transgenic mice. In this study, we have performed experiments in transgenic mice to determine which domains of E7 contribute to these in vivo properties. The human keratin 14 promoter was used to direct expression of mutant E7 genes to stratified squamous epithelia in mice. The E7 mutants chosen had either an in-frame **deletion** in the conserved region 2 (CR2) domain, which is required for binding of the

retinoblastoma tumor suppressor
protein (pRb) and pRb-like proteins, or an in-frame
deletion in the E7 CR1 domain. The CR1 domain contributes to
cellular transformation at a level other than pRb binding. Four lines of
animals transgenic for an HPV-16 E7 harboring a CR1 **deletion** and
five lines harboring a CR2 **deletion** were generated and were
observed for overt and histological phenotypes. A detailed time course
analysis was performed to monitor acute effects of wild-type versus mutant
E7 on the epidermis, a site of high-level expression. In the transgenic
mice with the wild-type E7 gene, age-dependent expression of HPV-16 E7
correlated with the severity of epidermal hyperplasia. Similar
age-dependent patterns of expression of the mutant E7 genes failed to
result in any phenotypes. In addition, the transgenic mice with a mutant
E7 gene did not develop tumors. These experiments indicate that binding
and inactivation of pRb and pRb-like proteins through the CR2 domain of E7
are necessary for induction of epidermal hyperplasia and carcinogenesis in
mouse skin and also suggest a role for the CR1 domain in the induction of
these phenotypes through as-yet-uncharacterized mechanisms.

L25 ANSWER 32 OF 52 MEDLINE DUPLICATE 9
AN 97415586 MEDLINE
DN 97415586
TI RRB1 and RRB2 encode maize retinoblastoma-related proteins that interact with a plant D-type cyclin and geminivirus replication protein.
AU Ach R A; Durfee T; Miller A B; Taranto P; Hanley-Bowdoin L; Zambryski P C; Gruissem W
CS Department of Plant and Microbial Biology, University of California, Berkeley 94720-3102, USA.
NC GM16915 (NIGMS)
SO MOLECULAR AND CELLULAR BIOLOGY, (1997 Sep) 17 (9) 5077-86.
Journal code: NGY. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-AF007793; GENBANK-AF007794; GENBANK-AF007795
EM 199711
EW 19971104
AB Unlike mammalian and yeast cells, little is known about how plants regulate G1 progression and entry into the S phase of the cell cycle. In mammalian cells, a key regulator of this process is the
retinoblastoma tumor suppressor
protein (RB). In contrast, G1 control in Saccharomyces cerevisiae
does not utilize an RB-like protein. We report here the cloning of cDNAs from two Zea mays genes, RRB1 and RRB2, that encode RB-related proteins. Further, RRB2 transcripts are alternatively spliced to yield two proteins with different C termini. At least one RRB gene is expressed in all the tissues examined, with the highest levels seen in the shoot apex. RRB1 is a 96-kDa nuclear protein that can physically interact with two mammalian DNA tumor virus oncoproteins, simian virus 40 large-T antigen and adenovirus E1A, and with a plant D-type cyclin. These associations are abolished by mutation of a conserved cysteine residue in RRB1 that is also essential for RB function. RRB1 binding potential is also sensitive to **deletions** in the conserved A and B domains, although differences
exist in these effects compared to those of human RB. RRB1 can also bind to the AL1 protein from tomato golden mosaic virus (TGMV), a protein which is essential for TGMV DNA replication. These results suggest that G1 regulation in plant cells is controlled by a mechanism which is much more similar to that found in mammalian cells than that in yeast.

L25 ANSWER 33 OF 52 MEDLINE DUPLICATE 10
AN 97248396 MEDLINE
DN 97248396
TI Accumulation of p53 induced by the adenovirus E1A protein requires regions involved in the stimulation of DNA synthesis.
AU Querido E; Teodoro J G; Branton P E
CS Department of Biochemistry, McGill University, Montreal, Quebec, Canada.
SO JOURNAL OF VIROLOGY, (1997 May) 71 (5) 3526-33.
Journal code: KCV. ISSN: 0022-538X.
CY United States

DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199707
EW 19970701
AB It has been known for some time that expression of the 243-residue (243R) human adenovirus type 5 (Ad5) early region 1A (E1A) protein causes an increase in the level of the cellular tumor suppressor p53 and induction of p53-dependent apoptosis. **Deletion** of a portion of conserved region 1 (CR1) had been shown to prevent apoptosis, suggesting that binding of p300 and/or the pRB **retinoblastoma tumor suppressor** and related **proteins** might be implicated. To examine the mechanism of the E1A-induced accumulation of p53, cells were infected with viruses expressing E1A-243R containing various **deletions** which have well-characterized effects on p300 and pRB binding. It was found that in human HeLa cells and rodent cells, complex formation with p300 but not pRB was required for the rise in p53 levels. However, in other human cell lines, including MRC-5 cells, E1A proteins which were able to form complexes with either p300 or pRB induced a significant increase in p53 levels. Only E1A mutants defective in binding both classes of proteins were unable to stimulate p53 accumulation. This same pattern was also apparent in p53-null mouse cells coinfected by Ad5 mutants and an adenovirus vector expressing either wild-type or mutant human p53 under a cytomegalovirus promoter, indicating that the difference in importance of pRB binding may relate to differences between rodent and human p53 expression. The increase in p53 levels correlated well with the induction of apoptosis and, as shown previously, with the stimulation of cellular DNA synthesis. Thus, it is possible that the accumulation of p53 is induced by the induction of unscheduled DNA synthesis by E1A proteins and that increased levels of p53 then activate cell death pathways.

L25 ANSWER 34 OF 52 MEDLINE
AN 97225933 MEDLINE
DN 97225933
TI Regulation of E2F through ubiquitin-proteasome-dependent degradation: stabilization by the pRB tumor suppressor protein.
AU Campanero M R; Flemington E K
CS Division of Tumor Virology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA 02115, USA.
NC R29 GM48045 (NIGMS)
CA47554 (NCI)
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1997 Mar 18) 94 (6) 2221-6.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199706
EW 19970604
AB The E2F family of transcription factors plays a key role in regulating cell-cycle progression. Accordingly, E2F is itself tightly controlled by a series of transcriptional and posttranscriptional events. Here we provide evidence that E2FI protein levels are regulated by the ubiquitin-proteasome-dependent degradation pathway. An analysis of E2F1 mutants identified a conserved carboxyl-terminal region, which is required for eliciting ubiquitination and protein turnover. Fusion of this E2F1 carboxyl-terminal sequence to a heterologous protein, GAL4, resulted in destabilization of GAL4. Previous studies identified an overlapping region of E2F1 that facilitates complex formation with **retinoblastoma tumor suppressor protein**, pRB, and we found that pRB blocks ubiquitination and stabilizes E2F1. These results suggest a new mechanism for controlling the cell-cycle regulatory activity of E2F1.

L25 ANSWER 35 OF 52 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1997:297881 BIOSIS
DN PREV199799597084
TI Induction of p16 during immortalization by HPV 16 and 18 and not during malignant transformation.

AU Nakao, Y.; Yang, X.; Yokoyama, M.; Ferenczy, A.; Tang, S.-C.; Pater, M. M.; Pater, A. (1)
CS (1) Dep. Obstetrics Gynecology, Saga Med. Sch., Saga 849 Japan
SO British Journal of Cancer, (1997) Vol. 75, No. 10, pp. 1410-1416. ISSN: 0007-0920.
DT Article
LA English
AB The p16 (MTS1) tumour-suppressor gene is a cyclin-dependent kinase (cdk) inhibitor that decelerates the cell cycle by inactivating the cdks that phosphorylate the retinoblastoma tumour-suppressor gene (Rb) protein (pRb). In cervical cancers, pRb is inactivated by the HPV E7 oncoprotein or by mutations. The hypothesis of earlier reports was that the disruption of the p16/cdk-cyclin/Rb cascade is essential for malignant cervical transformation/carcinogenesis. We previously established in vitro model systems of cervical cancer representing four steps of oncogenic progression initiated by the two most common oncogenic HPVs in ectocervical and endocervical epithelial cells. This report used these systems to investigate the role of p16 in cervical cancers. A dramatic enhancement of the p16 RNA level was observed after immortalization by HPV 16 or 18. Furthermore, the p16 protein was newly observed following immortalization. However, no further changes were found for RNA or protein levels after serum selection or malignant transformation. For three cervical carcinoma cell lines, similar high levels of p16 expression were seen. Point mutations or homozygous **deletions** of p16 were not observed in the in vitro systems or in clinical specimens. These results suggest that the inactivation of the p16/cdk-cyclin/Rb cascade does not occur during malignant transformation but occurs during the immortalization by HPV in HPV-harbouring premalignant lesions, the in situ equivalent of immortalized cells. Also suggested is that p16 has no role in the specific malignant transformation step from immortal premalignant lesions during the carcinogenesis of HPV-initiated cervical cancers.

L25 ANSWER 36 OF 52 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1997:152866 BIOSIS
DN PREV199799452069
TI E2F-1 cooperates with topoisomerase II inhibition and DNA damage to selectively augment p53-independent apoptosis.
AU Nip, John; Strom, David K.; Fee, Brian E.; Zambetti, Gerard; Cleveland, John L.; Hiebert, Scott W. (1)
CS (1) Dep. Biochemistry, Vanderbilt Univ. Sch. Med., Nashville, TN 37232-0146 USA
SO Molecular and Cellular Biology, (1997) Vol. 17, No. 3, pp. 1049-1056. ISSN: 0270-7306.
DT Article
LA English
AB Mutations in the retinoblastoma (pRb) tumor suppressor pathway including its cyclin-cdk regulatory kinases, or cdk inhibitors, are a hallmark of most cancers and allow unrestrained E2F-1 transcription factor activity, which leads to unregulated G-1-to-S-phase cell cycle progression. Moderate levels of E2F-1 overexpression are tolerated in interleukin 3 (IL-3)-dependent 32D.3 myeloid progenitor cells, yet this induces apoptosis when these cells are deprived of IL-3. However, when E2F activity is augmented by coexpression of its heterodimeric partner, DP-1, the effects of survival factors are abrogated. To determine whether enforced E2F-1 expression selectively sensitizes cells to cytotoxic agents, we examined the effects of chemotherapeutic agents and radiation used in cancer therapy. E2F-1 overexpression in the myeloid cells preferentially sensitized cells to apoptosis when they were treated with the topoisomerase II inhibitor etoposide. Although E2F-1 alone induces moderate levels of p53 and treatment with drugs markedly increased p53, the **deleterious** effects of etoposide in E2F-1-overexpressing cells were independent of p53 accumulation. Coexpression of Bcl-2 and E2F-1 in 32D.3 cells protected them from etoposide-mediated apoptosis. However, Bcl-2 also prevented apoptosis of these cells upon exposure to 5-fluorouracil and doxorubicin, which were also cytotoxic for control cells. Pretreating E2F-1-expressing cells with ICRF-193, a second topoisomerase II inhibitor that does not damage DNA, protected the cells from etoposide-induced apoptosis. However, ICRF-193 cooperated with DNA-damaging agents to induce apoptosis. Therefore, topoisomerase II inhibition and DNA damage can cooperate to selectively induce

p53-independent apoptosis in cells that have unregulated E2F-1 activity resulting from mutations in the pRb pathway.

L25 ANSWER 37 OF 52 MEDLINE DUPLICATE 11
AN 97293286 MEDLINE
DN 97293286
TI Current concepts in neuro-oncology: the cell cycle--a review.
AU Dirks P B; Rutka J T
CS Brain Tumor Research Laboratory, Hospital for Sick Children, University of Toronto, Ontario, Canada.
SO NEUROSURGERY, (1997 May) 40 (5) 1000-13; discussion 1013-5. Ref: 162
Journal code: NZL. ISSN: 0148-396X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199709
EW 19970904
AB Uncontrolled cellular proliferation is the hallmark of human malignant brain tumors. Their growth proceeds inexorably, in part because their cellular constituents have an altered genetic code that enables them to evade the checks and balances of the normal cell cycle. Recently, a number of major advances in molecular biology have led to the identification of several critical genetic and enzymatic pathways that are disturbed in cancer cells resulting in uncontrolled cell cycling. We now know that the progression of a cell through the cell cycle is controlled in part by a series of protein kinases, the activity of which is regulated by a group of proteins called cyclins. Cyclins act in concert with the cyclin-dependent kinases (CDKs) to phosphorylate key substrates that facilitate the passage of the cell through each phase of the cell cycle. A critical target of cyclin-CDK enzymes is the **retinoblastoma tumor suppressor protein**, and phosphorylation of this protein inhibits its ability to restrain activity of a family of transcription factors (E2F family), which induce expression of genes important for cell proliferation. In addition to the cyclins and CDKS, there is an emerging family of CDK inhibitors, which modulate the activity of cyclins and CDKs. CDK inhibitors inhibit cyclin-CDK complexes and transduce internal or external growth-suppressive signals, which act on the cell cycle machinery. Accordingly, all CDK inhibitors are candidate tumor suppressor genes. It is becoming clear that a common feature of cancer cells is the abrogation of cell cycle checkpoints, either by aberrant expression of positive regulators (for example, cyclins and CDKs) or the loss of negative regulators, including p21Cip1 through loss of function of its transcriptional activator p53, or **deletion** or mutation of p16ink4A (multiple tumor suppressor 1/CDKN2) and the **retinoblastoma tumor suppressor protein**. In this review, we describe in detail our current knowledge of the normal cell cycle and how it is disturbed in cancer cells. Because there have now been a number of recent studies showing alterations in cell cycle gene expression in human brain tumors, we will review the derangements in both the positive and negative cell cycle regulators that have been reported for these neoplasms. A thorough understanding of the molecular events of the cell cycle may lead to new opportunities by which astrocytoma cell proliferation can be controlled either pharmacologically or by gene transfer techniques.

L25 ANSWER 38 OF 52 MEDLINE DUPLICATE 12
AN 97405869 MEDLINE
DN 97405869
TI The phosphatase inhibitor okadaic acid stimulates the TSH-induced G1-S phase transition in thyroid cells.
AU Lazzereschi D; Coppa A; Minicione G; Lavitrano M; Fragomele F; Colletta G
CS Dipartimento di Medicina Sperimentale e Patologia, Facolt`a di Medicinae Chirurgia, Universit`a La Sapienza, Rome, Italy.
SO EXPERIMENTAL CELL RESEARCH, (1997 Aug 1) 234 (2) 425-33.
Journal code: EPB. ISSN: 0014-4827.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)

LA English
FS Priority Journals; Cancer Journals
EM 199711
AB Protein phosphorylation plays an essential role in regulating many cellular processes in eukaryotes. Signal transduction mechanisms that are reversibly controlled by protein phosphorylation require also protein phosphatases (PPs). Okadaic acid (OA), which is a potent inhibitor of protein phosphatase 2A (PP2A) and protein phosphatase 1, elicits phosphorylation of many proteins in unstimulated cells and induces different cellular responses, including transcriptional activation, shape changes, and pseudomitotic state. In this study, the effects of OA on rat thyroid cells (FRTL-5 strain) were analyzed to evaluate the role of serine/threonine phosphatases in hormone-induced thyroid cell proliferation. OA at a concentration range between 0.1 and 1 nM stimulated thyroid cell growth. Furthermore, 0.25 nM OA increased about 3.5-fold the thyrotropin (TSH)-induced DNA synthesis in quiescent cells. OA treatment also stimulated cell proliferation induced by drugs that mimic TSH effect, such as 8Br-cAMP and cholera toxin, suggesting that PP2A activity was relevant in the cAMP pathway activated by the hormone. Flow cytometry experiments showed that OA significantly increased the fraction of TSH-stimulated quiescent cells entering the S phase. In order to define the mechanisms underlying the observed stimulatory effect of OA on thyroid cell growth, expression of genes relevant in the G1-S phase transition was evaluated. A 2-fold increase in the level of cyclin D1 mRNA expression was found by Northern blot analysis in OA-treated cells. Although cdk2 gene expression was not modulated by the same OA treatment, an increase in Cdk2 protein was revealed by immunoprecipitation experiments. Moreover, OA **modifies** the phosphorylation pattern of the **tumor suppressor retinoblastoma protein**, a key event in the G1-S phase transition. Therefore, these experiments reveal that PP2A phosphatases play an important role in thyroid cell growth and can act at multiple sites in the TSH pathways driving cells to S phase.

L25 ANSWER 39 OF 52 MEDLINE DUPLICATE 13
AN 97405850 MEDLINE
DN 97405850
TI Inhibition of mouse thymidylate synthase promoter activity by the wild-type p53 tumor suppressor protein.
AU Lee Y; Chen Y; Chang L S; Johnson L F
CS Department of Molecular Genetics, Children's Hospital, The Ohio State University, Columbus 43210, USA.
NC GM29356 (NIGMS)
CA54323 (NCI)
SO EXPERIMENTAL CELL RESEARCH, (1997 Aug 1) 234 (2) 270-6.
Journal code: EPB. ISSN: 0014-4827.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199711
AB The p53 tumor suppressor protein is an important negative regulator of the G1 to S transition in mammalian cells. We have investigated the effect of p53 on the expression of the mouse thymidylate synthase (TS) gene, which normally increases as cells enter S phase. A luciferase indicator gene that was driven by the wild-type or various **modified** forms of the TATA-less mouse TS promoter was transiently cotransfected with a p53 expression plasmid into TS-deficient hamster V79 cells and the level of luciferase activity was determined. We found that wild-type p53 inhibited TS promoter activity by greater than 95% but had a strong stimulatory effect on an artificial promoter that contained multiple p53-binding sites. In contrast, an expression plasmid that encodes a mutant form of p53 or a wild-type **retinoblastoma tumor suppressor protein** had little effect on TS promoter activity. **Deletion** of sequences upstream or downstream of the TS essential promoter region, or inactivation of each of the known elements within the essential promoter region, had no effect on the ability of wild-type p53 to inhibit TS promoter activity. Our observations indicate that the inhibition of TS promoter activity by p53 is not due to the presence of a specific p53 negative response element in the TS promoter. Rather, it appears that p53 inhibits the TS promoter by sequestering

("squelching") one or more general transcription factors.

L25 ANSWER 40 OF 52 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1997:379157 BIOSIS
DN PREV199799678360
TI Nuclear tyrosine kinase c-Abl can mediate apoptosis in cells deficient for the **tumor suppressors** p53 and **retinoblastoma protein**.
AU Theis, S.; Roemer, K.
CS Abteilung Virologie, Univ. Saarlandes, Haus 47, D-66421 Homburg, Saar Germany
SO Journal of Molecular Medicine (Berlin), (1997) Vol. 75, No. 7, pp. B171.
Meeting Info.: XIX Symposium of the International Association for Comparative Research on Leukemia and Related Diseases Heidelberg, Germany July 13-18, 1997
ISSN: 0946-2716.
DT Conference; Abstract
LA English

L25 ANSWER 41 OF 52 USPATFULL
AN 96:58321 USPATFULL
TI E6 associated protein and methods of use thereof
IN Huibregtse, Jon M., Brighton, MA, United States
Scheffner, Martin, Walldorf, Germany, Federal Republic of
Howley, Peter M., Wellesley, MA, United States
PA United States of America, Washington, DC, United States (U.S. government)
PI US 5532348 19960702
AI US 1993-100692 19930730 (8)
DT Utility
EXNAM Primary Examiner: Jones, W. Gary; Assistant Examiner: Houtteman, Scott W.
LREP Townsend and Townsend and Crew
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN 21 Drawing Figure(s); 12 Drawing Page(s)
LN.CNT 1393
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides compositions of isolated and purified E6 Associated Protein and fragments thereof. Also provided are nucleic acid constructs encoding E6 Associated Protein. These compositions may be employed to identify compounds which inhibit binding of high risk HPV E6 to p53. The compositions of the present invention may also be used in methods to detect the presence of high risk HPV in biological samples.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L25 ANSWER 42 OF 52 MEDLINE DUPLICATE 14
AN 97098528 MEDLINE
DN 97098528
TI The tumorigenic potential and cell growth characteristics of p53-deficient cells are equivalent in the presence or absence of Mdm2.
AU Jones S N; Sands A T; Hancock A R; Vogel H; Donehower L A; Linke S P; Wahl G M; Bradley A
CS Department of Molecular and Human Genetics, Baylor College of Medicine, Houston, TX 77030, USA.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1996 Nov 26) 93 (24) 14106-11.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199703
EW 19970303
AB The Mdm2 oncoprotein forms a complex with the p53 tumor suppressor protein and inhibits p53-mediated regulation of heterologous gene expression. Recently, Mdm2 has been found to bind several other proteins that function to regulate cell cycle progression, including the E2F-1/DP1 transcription factor complex and the **retinoblastoma tumor-**

suppressor protein. To determine whether Mdm2 plays a role in cell cycle control or tumorigenesis that is distinct from its ability to modulate p53 function, we have examined and compared both the in vitro growth characteristics of p53-deficient and Mdm2/p53-deficient fibroblasts, and the rate and spectrum of tumor formation in p53-deficient and Mdm2/p53-deficient mice. We find no difference between p53-deficient fibroblasts and Mdm2/p53-deficient fibroblasts either in their rate of proliferation in culture or in their survival frequency when treated with various genotoxic agents. Cell cycle studies indicate no difference in the ability of the two cell populations to enter S phase when treated with DNA-damaging agents or nucleotide antimetabolites, and p53-deficient fibroblasts and Mdm2/p53-deficient fibroblasts exhibit the same rate of spontaneous immortalization following long-term passage in culture. Finally, p53-deficient mice and Mdm2/p53-deficient mice display the same incidence and spectrum of spontaneous tumor formation in vivo. These results demonstrate that **deletion** of Mdm2 has no additional effect on cell proliferation, cell cycle control, or tumorigenesis when p53 is absent.

L25 ANSWER 43 OF 52 MEDLINE DUPLICATE 15
AN 96278843 MEDLINE
DN 96278843
TI SV40 large T antigen transactivates the human cdc2 promoter by inducing a CCAAT box binding factor.
AU Chen H; Campisi J; Padmanabhan R
CS Department of Biochemistry and Molecular Biology, the University of Kansas Medical Center, Kansas City, Kansas 66160-7421, USA.
NC CA33099 (NCI)
AG09909 (NIA)
AG11658 (NIA)
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1996 Jun 14) 271 (24) 13959-67.
Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199610
AB Cyclin-dependent protein kinases (Cdks) play a key role in the cell division cycle of eukaryotic cells. Cdc2, the first mammalian Cdk that was discovered, is expressed in S phase and functions in the G2 to M phase transition. By transfecting segments of the human cdc2 promoter linked to a reporter gene into monkey kidney (CV-1) cells, we identified the region containing the Sp1, E2F, and two CCAAT box binding sites as essential and sufficient for basal transcription. SV40 large T antigen (SV40-LT) is a viral oncoprotein that transactivates viral and cellular promoters and induces DNA synthesis in quiescent cells. SV40-LT transactivated wild-type cdc2 promoter/reporter constructs in a dose-dependent manner, coinciding with an increase in endogenous cdc2 mRNA. A mutant promoter from which the two CCAAT box motifs were **deleted** was 8-fold less sensitive to SV40-LT. Activation by SV40-LT did not require its ability to bind the **retinoblastoma** or p53 **tumor suppressor proteins**. SV40-LT induced a specific CCAAT box-binding factor (CBF) in CV-1 and COS-7 cells, as judged by gel shift and Southwestern analyses. Similar results were obtained in human fibroblasts expressing a conditional SV40-LT. The SV40-LT-inducible CBF appears to be novel and differs from the CBF that activates heat shock protein 70 gene expression.

L25 ANSWER 44 OF 52 MEDLINE DUPLICATE 16
AN 96247496 MEDLINE
DN 96247496
TI Inactivation of multiple tumor-suppressor genes involved in negative regulation of the cell cycle, MTS1/p16INK4A/CDKN2, MTS2/p15INK4B, p53, and Rb genes in primary lymphoid malignancies.
AU Hangaishi A; Ogawa S; Imamura N; Miyawaki S; Miura Y; Uike N; Shimazaki C; Emi N; Takeyama K; Hirosawa S; Kamada N; Kobayashi Y; Takemoto Y; Kitani T; Toyama K; Ohtake S; Yazaki Y; Ueda R; Hirai H
CS Third Department of Internal Medicine, Faculty of Medicine, University of Tokyo, Tokyo, Japan.
SO BLOOD, (1996 Jun 15) 87 (12) 4949-58.
Journal code: A8G. ISSN: 0006-4971.

CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199610
AB It is now evident that the cell cycle machinery has a variety of elements negatively regulating cell cycle progression. However, among these negative regulators in cell cycle control, only 4 have been shown to be consistently involved in the development of human cancers as **tumor suppressors**: Rb (**Retinoblastoma** susceptibility **protein**), p53, and two recently identified cyclin-dependent kinase inhibitors, p16INK4A/MTS1 and p15INK4B/MTS2. Because there are functional interrelations among these negative regulators in the cell cycle machinery, it is particularly interesting to investigate the multiplicity of inactivations of these tumor suppressors in human cancers, including leukemias/lymphomas. To address this point, we examined inactivations of these four genes in primary lymphoid malignancies by Southern blot and polymerase chain reaction-single-strand conformation polymorphism analyses. We also analyzed Rb protein expression by Western blot analysis. The p16INK4A and p15INK4B genes were homozygously **deleted** in 45 and 42 of 230 lymphoid tumor specimens, respectively. Inactivations of the Rb and p53 genes were 27 of 91 and 9 of 173 specimens, respectively. Forty-one (45.1%) of 91 samples examined for inactivations of all four tumor suppressors had one or more abnormalities of these four tumor-suppressor genes, indicating that dysregulation of cell cycle control is important for tumor development. Statistical analysis of interrelations among impairments of these four genes indicated that inactivations of the individual tumor-suppressor genes might occur almost independently. In some patients, disruptions of multiple tumor-suppressor genes occurred; 4 cases with p16INK4A, p15INK4B, and Rb inactivations; 2 cases with p16INK4A, p15INK4B, and p53 inactivations; and 1 case with Rb and p53 inactivations. It is suggested that disruptions of multiple tumor suppressors in a tumor cell confer an additional growth advantage on the tumor.

L25 ANSWER 45 OF 52 MEDLINE DUPLICATE 17
AN 96220486 MEDLINE
DN 96220486
TI Inhibition of E2F activity by the cyclin-dependent protein kinase inhibitor p21 in cells expressing or lacking a functional retinoblastoma protein.
AU Dimri G P; Nakanishi M; Desprez P Y; Smith J R; Campisi J
CS Department of Cancer Biology, Life Sciences Division, Berkeley National Laboratory, University of California 94720, USA.
NC AG09909 (NIA)
AG11658 (NIA)
AG11066 (NIA)
SO MOLECULAR AND CELLULAR BIOLOGY, (1996 Jun) 16 (6) 2987-97.
Journal code: NGY. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199609
AB p21Sdi1/WAF1/Cip1 inhibits cyclin-dependent protein kinases and cell proliferation. p21 is presumed to inhibit growth by preventing the phosphorylation of growth-regulatory **proteins**, including the **retinoblastoma tumor suppressor protein** (pRb). The ultimate effector(s) of p21 growth inhibition, however, is largely a matter of conjecture. We show that p21 inhibits the activity of E2F, an essential growth-stimulatory transcription factor that is negatively regulated by unphosphorylated pRb. p21 suppressed the activity of E2F-responsive promoters (dihydrofolate reductase and cdc2), but E2F-unresponsive promoters (c-fos and simian virus 40 early) were unaffected. Moreover, the simian virus 40 early promoter was rendered p21 suppressible by introducing wild-type, but not mutant, E2F binding sites; p21 **deletion** mutants showed good agreement in their abilities to inhibit E2F transactivation and DNA synthesis; and E2F-1 (which binds pRb), but not E2F-4 (which does not), reversed both inhibitory effects of

p21. Despite the central role for pRb in regulating E2F, p21 suppressed growth and E2F activity in cells lacking a functional pRb. Moreover, p21 protein (wild type but not mutant) specifically disrupted an E2F-cyclin-dependent protein kinase 2-p107 DNA binding complex in nuclear extracts of proliferating cells, whether or not they expressed normal pRb. Thus, E2F is a critical target and ultimate effector of p21 action, and pRb is not essential for the inhibition of growth or E2F-dependent transcription.

L25 ANSWER 46 OF 52 MEDLINE DUPLICATE 18
AN 97051965 MEDLINE
DN 97051965
TI Skeletal muscle cells lacking the retinoblastoma protein display defects in muscle gene expression and accumulate in S and G2 phases of the cell cycle.
AU Novitch B G; Mulligan G J; Jacks T; Lassar A B
CS Department of Biological Chemistry and Molecular Pharmacology, Harvard Medical School, Boston, Massachusetts 02115, USA.
NC NO1-HD-6-2915 (NICHD)
SO JOURNAL OF CELL BIOLOGY, (1996 Oct) 135 (2) 441-56.
Journal code: HMV. ISSN: 0021-9525.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199702
AB Viral oncoproteins that inactivate the **retinoblastoma tumor suppressor protein** (pRb) family both block skeletal muscle differentiation and promote cell cycle progression. To clarify the dependence of terminal differentiation on the presence of the different pRb-related proteins, we have studied myogenesis using isogenic primary fibroblasts derived from mouse embryos individually deficient for pRb, p107, or p130. When ectopically expressed in fibroblasts lacking pRb, MyoD induces an aberrant skeletal muscle differentiation program characterized by normal expression of early differentiation markers such as myogenin and p21, but attenuated expression of late differentiation markers such as myosin heavy chain (MHC). Similar defects in MHC expression were not observed in cells lacking either p107 or p130, indicating that the defect is specific to the loss of pRb. In contrast to wild-type, p107-deficient, or p130-deficient differentiated myocytes that are permanently withdrawn from the cell cycle, differentiated myocytes lacking pRb accumulate in S and G2 phases and express extremely high levels of cyclins A and B, cyclin-dependent kinase (Cdk2), and Cdc2, but fail to readily proceed to mitosis. Administration of caffeine, an agent that **removes** inhibitory phosphorylations on inactive Cdc2/cyclin B complexes, specifically induced mitotic catastrophe in pRb-deficient myocytes, consistent with the observation that the majority of pRb-deficient myocytes arrest in S and G2. Together, these findings indicate that pRb is required for the expression of late skeletal muscle differentiation markers and for the inhibition of DNA synthesis, but that a pRb-independent mechanism restricts entry of differentiated myocytes into mitosis.

L25 ANSWER 47 OF 52 MEDLINE DUPLICATE 19
AN 96192060 MEDLINE
DN 96192060
TI The interferon-inducible growth-inhibitory p202 protein: DNA binding properties and identification of a DNA binding domain.
AU Choubey D; Gutterman J U
CS Department of Molecular Oncology, University of Texas M.D. Anderson Cancer Center, Houston, 77030, USA.
SO BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1996 Apr 16) 221 (2) 396-401.
Journal code: 9Y8. ISSN: 0006-291X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199608
AB p202 is an interferon-inducible protein whose expression in transfected

cells inhibits proliferation. p202 binds to the **retinoblastoma tumor suppressor protein** in vitro and in vivo and the transcription factors AP-1 c-Fos and c-Jun, NF-kappaB p50 and p65, and inhibits the transcriptional activity of these factors in vivo. Here we report that p202 nonspecifically binds to double-stranded DNA and to single-stranded DNA in vitro. Analysis with recombinant p202 revealed that DNA binding activity is intrinsic to p202. A C-terminal **deletion** mutant of p202 exhibited DNA-binding properties, indicating that the C-terminus is dispensable for DNA binding. We also found that underphosphorylated p202 efficiently binds to DNA. Our data suggest that DNA binding activity of p202 may contribute to its functions.

L25 ANSWER 48 OF 52 MEDLINE
AN 95268331 MEDLINE
DN 95268331
TI The **retinoblastoma tumor suppressor protein**.
AU Hinds P W
CS Department of Pathology, Harvard Medical School, Boston, Massachusetts 02115, USA..
SO CURRENT OPINION IN GENETICS AND DEVELOPMENT, (1995 Feb) 5 (1) 79-83. Ref: 41
Journal code: BJC. ISSN: 0959-437X.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199508
AB Loss of the retinoblastoma protein, pRb, appears to have a role in several human tumor types. Mice lacking pRb have been produced as models of human disease, but have a different spectrum of affected tissues. Recent work shows that the tumorigenic effects of pRb may be revealed only after additional genetic alterations, such as loss of p53. New targets/effectors of pRb have been identified recently, and the system of kinases that inactivate pRb is proving to be complex.

L25 ANSWER 49 OF 52 USPATFULL
AN 94:86502 USPATFULL
TI APC gene and nucleic acid probes derived therefrom
IN Albertsen, Hans, Salt Lake City, UT, United States
Anand, Rakesh, Cheshire, England
Carlson, Mary, Salt Lake City, UT, United States
Groden, Joanna, Salt Lake City, UT, United States
Hedge, Philip J., Cheshire, England
Joslyn, Geoff, Salt Lake City, UT, United States
Kinzler, Kenneth, Baltimore, MD, United States
Markham, Alexander F., Cheshire, England
Nakamura, Yusuke, Tokyo, Japan
Thliveris, Andrew, Salt Lake City, UT, United States
Vogelstein, Bert, Baltimore, MD, United States
White, Raymond L., Salt Lake City, UT, United States
PA The Johns Hopkins Univ., Baltimore, MD, United States (U.S. corporation)
The Univ. of Utah, Salt Lake City, UT, United States (U.S. corporation)
Imperial Chemical Industries, London, England (non-U.S. corporation)
Cancer Institute, Tokyo, Japan (non-U.S. corporation)
PI US 5352775 19941004
AI US 1991-741940 19910808 (7)
PRAI GB 1991-962 19910116
GB 1991-963 19910116
GB 1991-974 19910116
GB 1991-975 19910116
DT Utility
EXNAM Primary Examiner: Hill, Jr., Robert J.; Assistant Examiner: Carlson, K. Cochrane
LREP Banner, Birch, McKie & Beckett
CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN 50 Drawing Figure(s); 48 Drawing Page(s)

LN.CNT 2221
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A human gene termed APC is disclosed. Methods and kits are provided for assessing mutations of the APC gene in human tissues and body samples. APC mutations are found in familial adenomatous polyposis patients as well as in sporadic colorectal cancer patients. APC is expressed in most normal tissues. These results suggest that APC is a tumor suppressor.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L25 ANSWER 50 OF 52 MEDLINE DUPLICATE 20
AN 95065713 MEDLINE
DN 95065713
TI A mutational analysis of the amino terminal domain of the human papillomavirus type 16 E7 oncoprotein.
AU Brokaw J L; Yee C L; Munger K
CS Laboratory of Tumor Virus Biology, National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20892..
SO VIROLOGY, (1994 Dec) 205 (2) 603-7.
Journal code: XEA. ISSN: 0042-6822.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199502
AB The human papillomavirus type 16 (HPV-16) E7 oncoprotein shares structural and functional similarity with the adenovirus (Ad) E1A protein and the SV40 large tumor antigen (TAg). Like these other DNA tumor virus oncoproteins, HPV-16 E7 interacts with the "pocket proteins," a family of host cellular **proteins** that include the **retinoblastoma** **tumor suppressor protein** and can cooperate with the ras oncogene to transform primary rodent cells. Mutational analyses have indicated that amino acid sequences outside of the pRB binding region are also important for the cellular transformation property of HPV-16 E7. These sequences include an amino terminal domain of the E7 protein that is similar to a portion of conserved region 1 of Ad E1A. In this study it is shown that the homologous amino acid sequences in Ad E1A and SV40 TAg are functionally interchangeable with the amino terminal HPV-16 E7 domain in transformation assays. **Deletion** analysis across the amino terminus of HPV-16 E7 indicated that the overall integrity of the entire CR1 homology domain is important for the biological activity of the HPV E7 oncoprotein.

L25 ANSWER 51 OF 52 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1993:367280 BIOSIS
DN PREV199396052955
TI EBNA-5, an Epstein-Barr virus-encoded nuclear antigen, binds to the retinoblastoma and p53 proteins.
AU Szekely, Laszlo; Selivanova, Galina; Magnusson, Kristinn P.; Klein, George; Wiman, Klas G.
CS Dep. Tumor Biol., Karolinska Inst., Box 60400, S-104 01 Stockholm Sweden
SO Proceedings of the National Academy of Sciences of the United States of America, (1993) Vol. 90, No. 12, pp. 5455-5459.
ISSN: 0027-8424.
DT Article
LA English
AB Epstein-Barr virus (EBV) immortalized human lymphoblastoid cell lines express six virally encoded nuclear proteins, designated EBV nuclear antigens 1-6 (EBNA-1-6). We show that the EBNA-5 protein (alternatively designated EBNA-LP) that is required for B-cell transformation can form a molecular complex with the **retinoblastoma** (RB) and p53 **tumor suppressor proteins**. Using EBNA-5 **deletion** mutants, we have found that a 66-amino acid-long peptide, encoded by the W repeat of the EBV genome, is sufficient for binding. Point mutations of RB and p53 that inhibit their complexing with other DNA viral oncoproteins do not affect their binding to EBNA-5. p53 competes with RB for EBNA-5 binding. Our data suggest that the mechanisms involved in EBV transformation may include impairment of RB and p53 function.

L25 ANSWER 52 OF 52 MEDLINE DUPLICATE 21

AN 93149605 MEDLINE
DN 93149605
TI Inhibition of histone H1 kinase expression, retinoblastoma protein phosphorylation, and cell proliferation by the phosphatase inhibitor okadaic acid.
AU Schonthal A; Feramisco J R
CS Department of Medicine, University of California, San Diego, La Jolla 92093-0636.
SO ONCOGENE, (1993 Feb) 8 (2) 433-41.
Journal code: ONC. ISSN: 0950-9232.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199305
AB Phosphorylation events are major regulatory mechanisms of signal transduction pathways that regulate gene expression and cell growth. To study the potential involvement of serine-threonine specific phosphatases in these processes we used okadaic acid (OA), an inhibitor of type 1 and type 2A protein phosphatases. Here we present evidence that OA arrests cells at defined points in the cell cycle. Concomitantly, expression and associated histone H1 kinase activity of cdc2 and cyclin A, two cell cycle regulatory proteins, are repressed by this agent. Furthermore, phosphorylation of the **tumor suppressor protein retinoblastoma**, an event thought to be necessary in order to permit cells to proliferate, is inhibited when OA is present. These effects are fully reversible since **removal** of OA restores cdc2 and cyclin A expression as well as histone H1 kinase activity, and the cells resume growth. Since cdc2 and cyclin A have previously been shown to be absolutely required for cell cycle progression it is likely that blockage of synthesis of these components contributes to the cytostatic effects of OA. Furthermore, our results suggest a positive role for OA sensitive protein phosphatases in the regulation of expression of these cell cycle regulatory proteins.

=> d bib abs hitstr

L11 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2000 ACS
AN 1998:604926 HCAPLUS
DN 129:211705
TI Analogs of the retinoblastoma tumor suppressor protein for use in treatment of hyperproliferative disorders
IN **Xu, Hong-ji; Hu, Shi-xue; Benedict, William F.** ; **Zhou, Yunli**
PA Board of Regents, the University of Texas System, USA; Baylor College of Medicine
SO PCT Int. Appl., 250 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9837091	A2	19980827	WO 1998-US3041	19980219
WO 9837091	A3	19981105		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9866573	A1	19980909	AU 1998-66573	19980219
EP 975750	A2	20000202	EP 1998-908570	19980219

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

PRAI US 1997-38118 19970220
WO 1998-US3041 19980219

AB Analogs of the retinoblastoma tumor suppressor protein Rb that are active in a broad range of cell types and that have a similar or higher biol. activity than the corresponding wild-type retinoblastoma tumor suppressor protein are described. In particular, deletions and mutations affecting the N-terminal region alter the activity of the protein. These analogs can be used to treat diseases characterized by abnormal cellular proliferation, including cancer. CDNAS for a series of N-terminal and internal deletion analogs of the Rb protein were constructed by std. methods and expression vectors for these cDNAs were introduced into a Rb protein-deficient bladder carcinoma cell line using a tetracycline-regulated expression system. Several of the analogs dramatically reduced DNA synthesis in transformed cells after tetracycline induction of expression. Development of a tightly-regulated tetracycline-induced regulatory system for the Rb and p53 genes is described. Stably transformed clones carrying a tetracycline-regulated expression construct derived from a wide variety of tumor cell lines were established. Induction of expression led to a rapid and irreversible cessation of growth and of DNA synthesis. This effect was tumor-specific.

IT **120178-12-3,** Telomerase
RL: BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(Rb protein analog inhibition of; analogs of retinoblastoma tumor suppressor protein for use in treatment of hyperproliferative disorders)
RN 120178-12-3 HCAPLUS
CN Nucleotidyltransferase, terminal deoxyribo- (telomeric DNA) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **212254-12-1 212254-15-4 212254-17-6**
212254-23-4 212254-25-6 212254-29-0
212254-31-4 212254-34-7 212254-36-9
212254-38-1 212254-41-6 212254-43-8
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(amino acid sequence; analogs of retinoblastoma tumor suppressor protein for use in treatment of hyperproliferative disorders)
RN 212254-12-1 HCAPLUS
CN 34-928-Rb protein [34-methionine](human clone pCMVRBd2-34) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 212254-15-4 HCAPLUS
CN 54-928-Rb protein [54-methionine](human clone pCMVRBd2-55) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 212254-17-6 HCAPLUS
CN 77-928-Rb protein [77-methionine](human clone pCMVRBd2-78) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 212254-23-4 HCAPLUS
CN 96-928-Rb protein [96-methionine](human clone pCMVRBd2-97) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 212254-25-6 HCAPLUS
CN 148-928-Rb protein (human clone pCMVRBd1-147) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 212254-29-0 HCAPLUS
CN (1-30)-(108-928)-Rb protein (human clone pRB.DELTA.31-107) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 212254-31-4 HCAPLUS
CN (1-76)-(108-928)-Rb protein (human clone pRB.DELTA.77-107) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 212254-34-7 HCAPLUS
CN Rb Protein [111-glycine,112-aspartic acid] (human clone pRBm111/112) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 212254-36-9 HCAPLUS
CN (1-110)-(181-928)-Rb protein (human clone pRB.DELTA.111-181) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 212254-38-1 HCAPLUS
CN (1-110)-(242-928)-Rb protein (human clone pRB.DELTA.111-241) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 212254-41-6 HCAPLUS
CN (1-180)-(242-928)-Rb protein (human clone pRB.DELTA.181-241) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 212254-43-8 HCAPLUS
CN (1-241)-(301-928)-Rb protein (human clone pRB.DELTA.242-300) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **212254-14-3 212254-16-5 212254-22-3**
212254-24-5 212254-26-7
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nucleotide sequence; analogs of retinoblastoma tumor suppressor protein for use in treatment of hyperproliferative disorders)
RN 212254-14-3 HCAPLUS
CN DNA (human clone pCMVRBd2-34 34-928-Rb protein [34-methionine]-specifying) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 212254-16-5 HCAPLUS
CN DNA (human clone pCMVRBd2-55 54-928-Rb protein [54-methionine]-specifying) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 212254-22-3 HCAPLUS
CN DNA (human clone pCMVRBd2-78 77-928-Rb protein [77-methionine]-specifying) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 212254-24-5 HCAPLUS
CN DNA (human clone pCMVRBd2-97 96-928-Rb protein [96-methionine]-specifying) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 212254-26-7 HCAPLUS
CN DNA (human clone pCMVRBd1-147 148-928-Rb protein-specifying) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **212254-27-8 212254-30-3 212254-32-5**
212254-35-8 212254-37-0 212254-39-2
212254-42-7
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nucleotide sequence; analogs of retinoblastoma tumor suppressor protein for use in treatment of hyperproliferative disorders)
RN 212254-27-8 HCAPLUS
CN DNA (human clone pRB.DELTA.31-107 (1-30)-(108-928)-Rb protein-specifying) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 212254-30-3 HCAPLUS
CN DNA (human clone pRB.DELTA.77-107 (1-76)-(108-928)-Rb protein-specifying) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 212254-32-5 HCAPLUS
CN DNA (human clone pRBm111/112 Rb Protein [111-glycine,112-aspartic acid]-specifying) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 212254-35-8 HCAPLUS
CN DNA (human clone pRB.DELTA.111-181 (1-110)-(181-928)-Rb protein-specifying) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 212254-37-0 HCAPLUS
CN DNA (human clone pRB.DELTA.111-241 (1-110)-(242-928)-Rb protein-specifying) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 212254-39-2 HCAPLUS
CN DNA (human clone pRB.DELTA.181-241 (1-180)-(242-928)-Rb protein-specifying) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 212254-42-7 HCAPLUS
CN DNA (human clone pRB.DELTA.242-300 (1-241)-(301-928)-Rb protein-specifying) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***